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SELECTED ION FRAGMENTATION WITH A

TRIPLE QUADRUPOLE MASS SPECTROMETER.

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A triple quadrupole mass spectrometer (TQMS) has been designed and developed for the direct analysis of mixtures and the elucidation of molecular structures. In the TQMS, several ionic species are generated from a sample, ions of a particular mass are selected for fragmentation, and the resulting fragment ions are mass analyzed. The instrument consists of, in series, a dual chemical ionization/electron impact (CI/EI) ionization source, a quadrupole mass filter, an RF-Only quadrupole that can be

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pressurized with a collision gas, a second quadrupole mass filter, and an electron multiplier. The ion fragmentation process is performed by collision-induced dissociation (CID) in the RF-only quadrupole collision chamber. The instrument is described and its performance evaluated.

For structure elucidation, the formation and fragmentation of every fragment ion from a compound can be directly determined. A number of examples of the use of selected ion fragmentation for structure elucidation are presented, including a detailed study of the fragmentation of nonan-4-one. For mixture analysis, the first mass analyzer can separate the mixture components as their molecular ions, produced by soft ionization (e.g., CI) of the sample. The fragmentation spectra of the individual components can then be obtained by fragmenting the selected molecular ions and scanning the second analyzer. The identification of isomeric and isobaric compounds in a mixture is demonstrated. Detection limits of 10^{-15} mole for methane and nitrobenzene are shown.

The low-energy CID process which occurs in the center quadrupole is characterized. The low-energy process (10-20 eV ion kinetic energy) probably occurs by direct vibrational excitation through momentum transfer. The effect of collision gas identity and pressure, and ion kinetic energy on the collision process is also discussed.

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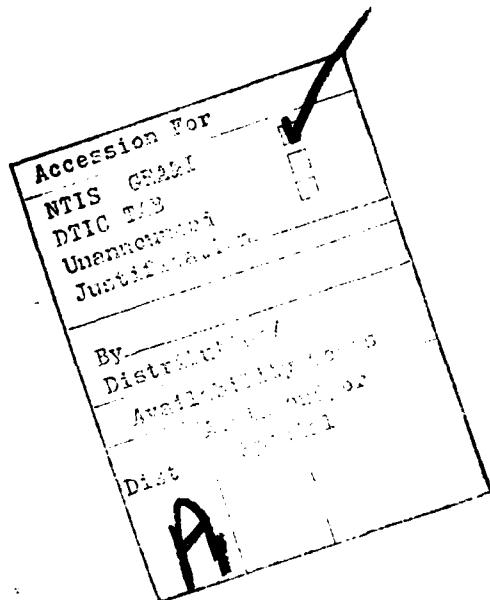
ABSTRACT

SELECTED ION FRAGMENTATION WITH A
TRIPLE QUADRUPOLE MASS SPECTROMETER

By

Richard Alan Yost

A triple quadrupole mass spectrometer has been designed
and developed for the direct analysis of mixtures and the
elucidation of molecular structures. The triple quadru-
pole system is a simple and efficient implementation of the
selected ion fragmentation technique, whereby several
ionic species are generated from a sample, ions of a
particular mass are selected for fragmentation, and the
resulting fragment ions are mass analyzed. The instrument
consists of, in series, a dual chemical ionization/electron
impact (CI/EI) ionization source, a quadrupole mass filter,
an RF-only quadrupole that can be pressurized with a
collision gas, a second quadrupole mass filter, and an
electron multiplier. The ion fragmentation process is
performed by collision-induced dissociation (CID), in
which the ion acquires internal energy by collision with
a neutral molecule. The RF-only quadrupole collision
chamber provides focusing of scattered ions. In this

instrument the selected ion fragmentation process can provide enhanced selectivity and discrimination over normal mass spectrometry without significant loss of sensitivity. The instrument is described and its performance evaluated.

There are several applications of mass spectrometry which benefit greatly from the added information contained in the fragmentation spectrum of each ionic species produced in the source, including the elucidation of molecular structures and the analysis of mixtures. For structure elucidation, the formation and fragmentation of every fragment ion from a compound can be directly determined. A number of examples of the use of selected ion fragmentation for structure elucidation are presented, including a detailed study of the fragmentation of nonan-4-one. Over 400 distinct fragmentations of the molecule are observed, providing valuable information about the fragmentation pathways of the molecule and the structure of the various fragment ions.

For mixture analysis, the first mass analyzer can separate the mixture components as their molecular ions, produced by soft ionization (e.g., CI) of the sample. The fragmentation spectra of the individual components can then be obtained by fragmenting the selected molecular ions and scanning the second analyzer. The mixture analysis technique is discussed and specific application examples

are presented. The identification of isomeric and isobaric compounds in a mixture is demonstrated. Detection limits of 10^{-15} mole for methane and nitrobenzene are shown. Chemical noise is virtually eliminated by the selection of both parent and fragment ion.

The low-energy CID process which occurs in the center quadrupole is characterized. It is shown to be a highly efficient process for the fragmentation of organic ions. The low-energy process (10-20 eV ion kinetic energy) probably occurs by direct vibrational excitation through momentum transfer, and is a very different process from the electronic excitation process which occurs at high kinetic energy (3-20 keV). The collision of CCl^+ with several collision gases produces not only fragment ions but also charge exchange ions and addition products. The ion products with Ar as collision gas include C^+, Cl^+, Ar^+, CAr^+, and $ClAr^+$. The effect of collision gas identity and pressure, and ion kinetic energy on the collision process is also discussed. The characterization of the CID process provides information of fundamental interest as well as making possible the efficient use of the process for chemical analysis.

Triple quadrupole mass spectrometry is shown to be a powerful new technique for mixture analysis and structure elucidation. The simplicity and versatility of the technique, combined with its sensitivity and potential for chemical analysis, all point to a bright future.

SELECTED ION FRAGMENTATION WITH A

TRIPLE QUADRUPOLE MASS SPECTROMETER

By

Richard Alan Yost

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recognized.

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CHAPTER 1

INTRODUCTION

This thesis is a description of the design and characterization of a new triple quadrupole mass spectrometer and its application to problems of mixture analysis and structure elucidation. We first introduced the concept of selected ion fragmentation with a triple quadrupole mass spectrometer based on preliminary experiments performed in 1977 at La Trobe University in Australia (1). A second publication based on the Australia experiments describes the characterization of the highly efficient low-energy collision process (2). The reader is referred to these two publications (reprinted in the Appendices) for information regarding the preliminary experiments on the La Trobe instrument. The experiments described in the following chapters were all performed on the instrument developed at Michigan State University, which is described in Chapter 5.

Organization of the Thesis

The thesis is divided into six chapters. This introductory chapter provides background information to help the reader understand the arrangement and significance

of the research described in succeeding chapters. This
includes a perspective on the field of mass spectrometry,
a review of triple quadrupole mass spectrometry, and a
description of the operational modes and applications of
the instrument.

Chapter 2 describes the characterization of the low-
energy collision process which occurs in the center quad-
rupole. A brief overview of collision processes in mass
spectrometry is followed by a discussion of the effect of
experimental parameters on the low-energy collision process.
This characterization not only sheds some light on the funda-
mental nature of the collisional process, but also provides
the necessary background for the analytical application of
the technique.

The third chapter is a brief description of the mix-
ture analysis capabilities of the triple quadrupole system.
This chapter, in combination with Chapter 5, comprises a
paper submitted for publication. A description of an
earlier mixture analysis application appears in the Journal
of the American Chemical Society (1).

The technique of structure elucidation with the triple
quadrupole system is described in Chapter 4. This chapter
has been prepared for publication in two parts, an overview
of the technique, and a description of the nonan-4-one
experiments. Another example of a structure elucidation
problem appears in Chapter 5.

The fifth chapter is a description of the triple quadrupole instrument constructed at Michigan State University, and a detailed study of its performance. This chapter has been submitted for publication, and was also presented at a poster session at the 27th Annual Conference on Mass Spectrometry and Allied Topics in Seattle, June 1979.

The final chapter includes a statement of the conclusions of this work and an outlook on the future of triple quadrupole mass spectrometry.

Selected Ion Fragmentation Concept

One of the most active research areas in mass spectrometry today is selected ion fragmentation, in which several ionic species are generated from a sample, ions of a particular mass-to-charge (m/z) are selected for fragmentation, and the resulting fragment ions are mass-analyzed. The fragmentation can occur unimolecularly or as a result of collision-induced dissociation (CID) with residual gas molecules. Because the technique requires two stages of mass separation in tandem (one to select the parent ion and one to analyze the daughter ions resulting from fragmentation), it has also been dubbed MS/MS. The process of determining the fragmentation of mass-

selected ions can provide an added dimension of information about a sample compared to conventional mass spectrometric techniques.

Perspective on Mass Spectrometry

Mass spectrometry was introduced in 1913 (3), but did not come into common usage until the 1950's when interest in the quantitative analysis of petroleum fractions spurred its commercial development. Early mass spectrometers were all magnetic sector instruments. Double focusing instruments, in which an electric sector is added in order to focus ions of varying kinetic energy into the magnetic sector, were developed to increase the available mass resolution. It was not until the late 1950's that the quadrupole mass filter was proposed (4), and not until the 1960's were quadrupole instruments commercially available. The mass filter, as its name implies, allows ions of a chosen m/z to pass, while rejecting all others. It is constructed of four parallel rods with diagonally opposed pairs coupled together and an RF potential applied between the pairs. Under these conditions all ions experience stable trajectories and are transmitted. If DC potentials of opposite sign are applied to the pairs of rods as well, only those ions falling in a window of m/z valves are transmitted, and lighter or

heavier ions experience unstable trajectories and are lost.
A quadrupole mass spectrometer includes an ion source and
an ion detector positioned on either end of the mass
filter.

Despite the fact that the mass spectrometer was com-
mercially developed for the quantitation of relatively
complex mixtures, in qualitative studies even low levels
of impurities can make identification of a sample impos-
sible. For this reason, in the late 1950's the gas chromato-
graph was coupled to the mass spectrometer (GC/MS) to effect
prior separation of multicomponent mixtures (5). Coupling
of liquid chromatography to mass spectrometry (LC/MS) has
generated considerable interest recently (6) because it
minimizes the problems with thermally labile or involatile
samples associated with GC. Chromatography provides an
extra dimension of information when mass spectra are taken
at each retention time interval. However, when mixture
separation is performed chromatographically, the time
required to separate a component of interest can be need-
lessly long.

In structure elucidation applications, an extra dimen-
sion of information can be provided by the detection of
"metastable" ions (ions which are stable only long enough
to leave the ion source, and then decompose unimolecularly
before analysis). The use of metastable peaks to determine
specific fragmentation paths was first suggested in 1945 (7).

The use of metastable data for structure elucidation was extended dramatically with the development of Mass-Analyzed Ion Kinetic Energy Spectrometry, or MIKES (8). MIKES makes use of double-focusing mass spectrometers in which the ions are mass-analyzed by a magnetic sector before fragmentation, and the kinetic energy of the resulting ions is analyzed by a succeeding electric sector. This kinetic energy analysis of the ions can provide information on their m/z and the energy released on fragmentation. The added dimension of information that results not only provides valuable assistance in the elucidation of molecular structure, but can also make possible the separation and analysis of mixture components.

The most straightforward approach to providing an added dimension of mass spectral information is tandem mass spectrometry (MS/MS), in which two mass analyzers are connected in series. Lindholm in 1954 introduced the concept of using a tandem mass spectrometer with a collision chamber between the analyzers to study ion-molecule reactions (9). A dozen or more researchers are now using tandem instruments for this purpose (10). Most of these are tandem sector instruments, although a few tandem quadrupole instruments have been built and applied to ion-molecule reactions (11) and to photodissociation of ions (12,13). Tandem mass spectrometers designed for analytical applications of selected ion fragmentation are currently

under development or are operating in the laboratories
of Cooks, Hunt, and McLafferty. The work described in this
thesis, however, constitutes the first application of tandem
quadrupole mass spectrometry to problems in chemical anal-
ysis, and in particular, the first use of collision-induced
dissociation within a quadrupole field.

Overview of Triple Quadrupole Mass Spectrometry

The triple quadrupole mass spectrometer developed at
Michigan State University uses tandem quadrupole mass
filters to provide two stages of mass analysis. The center
RF-only quadrupole, positioned between the mass filters,
has no mass filtering action, but rather provides strong
focusing of the ions during fragmentation. The combina-
tion of three quadrupoles produces a simple and efficient
MS/MS instrument for selected ion fragmentation.

Triple quadrupole instruments were independently
designed and constructed for photodissociation studies by
two groups in the early 1970's (12,13). It was on one of
these instruments, in the laboratory of J. D. Morrison at
La Trobe University, that I performed the preliminary
experiments described in our earliest papers (1,2). In
the photodissociation experiments, the mass-selected ions
in the center quadrupole are excited by interaction with

photons from a dye laser or xenon lamp. The light absorbance is too low to measure, but the resulting fragment ions can be detected. In this way it is possible to study the optical spectroscopy of ions in the gas phase, and to study the fragmentation process using a monoenergetic source of excitation. The photofragmentation efficiency is extremely low, however, and even at low residual pressures (10^{-8} torr), the photodissociation signal is swamped by the collision-induced dissociation products. By increasing the pressure in the center quadrupole, this troublesome interference becomes a highly efficient fragmentation technique for analytical applications.

The instrument developed at Michigan State University consists of, in series, an ionization source, a quadrupole mass filter, an RF-only quadrupole collision chamber, another mass filter, and an ion detector. The selected ions are fragmented between the mass filters by collision-induced dissociation (CID) at low kinetic energies of 10-20 eV. The parent ions may be produced by ionization with or without significant fragmentation from gaseous, liquid, and solid samples. Mass analysis over the range 1 to 1000 amu is possible, with resolution of 1 part in 1500. The entire instrument is designed for ease of computer control. Only under complete control of micro- and mini-computers will the ultimate potential of the system for chemical analysis be realized.

Modes of Operation and Application

There are several possible modes of operation for the
triple quadrupole mass spectrometer, as described in
Chapter 5. Each of these modes finds application in the
solution of specific analytical problems.

The triple quadrupole instrument may be used as a
single stage mass spectrometer by scanning the first mass
filter with the second and third mass filters in RF-only
(total ion) mode. In this way the instrument may be applied
to problems which do not require the added dimension of
selected ion fragmentation. This mode can also be used
to tune the first quadrupole to the parent peak which is
to be fragmented.

For analysis of mixtures, the molecular ions for
all components can be produced by a soft ionization tech-
nique which produces very little fragmentation (e.g.,
chemical ionization), and can then be separated by the
first mass analyzer. For one component at a time, the
molecular ion can be selected with the first quadrupole,
fragmented in the second, and the mass spectrum obtained
by scanning the third. If the application requires only
the detection of a single component of interest, single
reaction monitoring may be employed, in which the first
and third quadrupoles are set to select a specific parent
ion/daughter ion pair. If several compounds are to be

detected, then several parent/daughter ion pairs may be selected in sequence using multiple reaction monitoring. A potentially powerful technique for analysis of mixture components is to scan the first and third quadrupoles with a fixed difference in mass. In this way a selected neutral loss which is characteristic of a specific functional group may be monitored, and mixture components which contain that group identified. In a similar way, the molecular ions may be monitored which contain a functional group that forms a specific addition product with a selected reactive collision gas.

A special case of mixture analysis is the identification of isotope labelling in samples with less than complete isotopic substitution. The first quadrupole can be set to mass select only those ions which do contain the isotope label(s), and can therefore eliminate the interference from the unlabelled ions.

All of the operational modes described for mixture analysis may also be used in solving problems of structure elucidation. In one mode, any fragment ion in a compound's normal mass spectrum may be mass selected by the first quadrupole. The selected fragment can be further fragmented by collision, and the spectrum of resulting ions obtained by scanning the third quadrupole. In this way the mass spectrum of a particular portion or functional moiety of a molecule can be determined. Alternatively,

all fragments which may further fragment to yield a specific
ion may be determined by scanning the first quadrupole
with the third set for that ion. Neutral loss spectrometry
is realized by scanning the two mass filters with a fixed
difference in mass, and thus those ions which show loss
of a specific neutral may be determined. The availability
of several modes of operation makes the triple quadrupole
mass spectrometer a versatile instrument for both struc-
ture elucidation and mixture analysis. These same modes
may be implemented with MIKES instruments; however, they
are much simpler in the triple quadrupole due to the in-
dependence of the two stages of mass separation.

There are many indications that triple quadrupole
mass spectrometry will prove to be a significant advance
in the field of mass spectrometry due to its simplicity,
its efficiency and sensitivity, and its potential for
chemical analysis. These indications include the wide-
spread interest in the technique at recent scientific
meetings and the evaluations of major figures in the
mass spectrometry field. The commercial development of
triple quadrupole instruments is very likely, and the
resulting widespread availability of the technique would
further increase the impact of triple quadrupole mass
spectrometry on chemical analysis.

CHAPTER 2

LOW-ENERGY COLLISION PROCESSES

Characterization of the low-energy collision processes which occur in the center quadrupole is an important step in the development of the triple quadrupole mass spectrometer. This characterization is important both as a fundamental study of the processes and as a method for optimization of the sensitivity and selectivity of the analytical technique.

Collision Processes in Mass Spectrometry

The role of collision processes has been of concern to mass spectrometrists for a number of years. Indeed, signals corresponding to collision-induced dissociation (the so-called "Aston bands") were observed in the very first mass spectra (3). Since that time there has been a great deal of interest in the collisions between ions and molecules, especially in the fundamental nature of the ion-molecule reaction. Major treatises have been written on the nature of ion-molecule reactions for simple molecules (14). From the study of ion-molecule reactions, the important analytical technique of chemical ionization was

developed in the mid-1960's (15).

Another important analytical technique which evolved from these studies was the use of collision-induced dissociation (CID) or collisional activation (CA) for fragmentation of selected ions as a complementary technique to unimolecular decompositions (metastable studies). The widespread use of the CID technique was catalyzed by a paper of Jennings in 1968 (16). Most of this CID work has been performed by Mass-Analyzed Ion Kinetic Energy Spectrometry (MIKES) with reversed-geometry double focusing mass spectrometers. The present work extends the use of CID to the triple quadrupole system.

The ion-molecule collisions in MIKES instruments occur at relatively high ion kinetic energies of 3-10 keV. At these energies the conversion of kinetic into internal energy occurs primarily by a vertical Franck-Condon type of electronic excitation. Fragmentation may occur after the ion and molecule are again separated, through relaxation of the electronic energy into vibrational levels (17). Because the electronic excitation occurs over a time interval much shorter than vibrational periods, the ion and molecule each retain their identity afterwards, and collision products due to attachment and displacement reactions are not formed. Ions due to changes in the electric charge of the ion and molecule can be produced, however, including products of charge exchange and charge

inversion. Although charge inversion products have been detected in MIKES experiments (18), the collision gas ions which result from charge exchange would not be analyzed even if they managed to enter the second sector. Nevertheless, charge exchange can cause a loss of ion signal. Indeed, the cross section for charge exchange and scattering can be relatively large compared to the cross section for fragmentation, and the resultant loss of ion signal can limit the sensitivity of the MIKES technique (19).

The collision processes observed in the triple quadrupole system are very different from those seen in MIKES instruments. The kinetic energy of the ions in the center quadrupole (typically 10-20 eV) is two to three orders of magnitude less than that in MIKES experiments. At these low energies the cross section for electronic excitation is quite low. Fragmentation probably occurs through direct vibrational excitation as a result of momentum transfer (17). Because the ion and molecule may "stick" together for a reasonably long time (several vibrational periods), product ions may result from addition or displacement reactions. Charge exchange product ions from the collision gas may also result. At high pressures, the product ion from a collision may undergo a second collision and be further changed. In those experiments where it is necessary that the observed product ions be the result of only single collisions, it is important to maintain a low

collision gas pressure, typically below 10^{-5} torr.

Examples of the types of collision products that are observed with the triple quadrupole mass spectrometer are depicted in Figure 2-1. The collision spectra are those observed when $^{35}ClC^+$ ions from CCl_4 are collided with various gases at approximately 10^{-3} torr and 10 eV axial kinetic energy. In addition to the CCl^+ reactant ion, three types of product ions are observed. Both possible fragment ions (C^+ and Cl^+) are formed with all five collision gases. In addition, charge exchange products are seen with all the collision gases except helium. Examples are Ar^+, H_2O^+, and N^+ and N_2^+. Helium has the highest ionization potential and would be the least likely to undergo charge exchange. A third class of ions, addition products, are also observed. Collision with argon, for example, produces ArC^+ and $ArCl^+$; with nitrogen, CN^+, CN_2^+, ClN^+, and $CClN^+$ are formed. These ion complexes are stable long enough to reach the detector approximately 50 μs after formation. These results, and those which follow, reinforce the conclusion that the low-energy collision process is a very different one from that observed in MIKES.

ION-MOLECULE REACTIONS OF CCl⁺
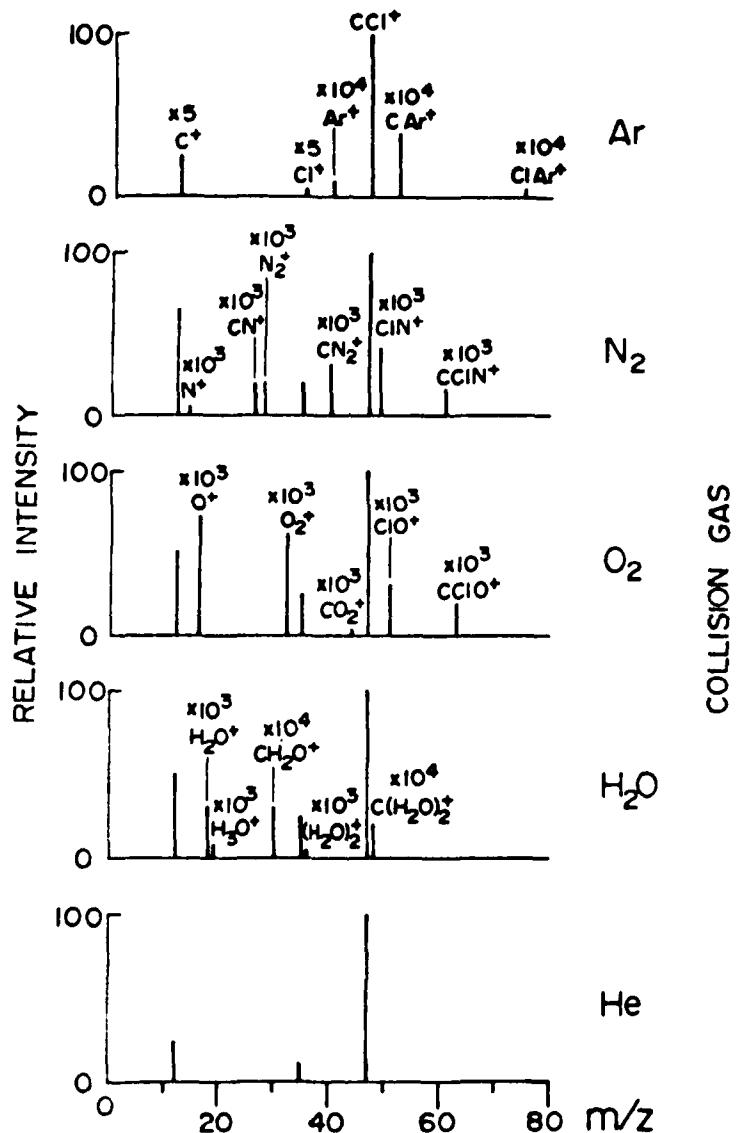
Figure 2-1. Ion-molecule reactions of $^{35}ClC^+$ with various collision gases.

Effect of Experimental Parameters on

Low-Energy CID

A major part of the characterization of the low-energy CID process is the study of the effects of varying the experimental parameters. We have already reported the results of a preliminary study of these effects on the triple quadrupole system at La Trobe University (2). This publication is reprinted in Appendix B. The effects of collision gas identity, collision gas pressure, and ion kinetic energy (axial and transverse) will be discussed in the sections which follow.

Collision Gas Species

An example of the effect that collision gas identity can have on the fragmentation process is shown by the CCl^+ study in Figure 2-1. The intensities of the C^+ and Cl^+ fragment ions relative to each other, and to the unfragmented CCl^+ peak, vary with different collision gases. The collision-gas peaks which result from charge exchange vary from relatively intense for N_2, O_2, and H_2O, to weak for Ar, to undetectable for He. Addition product ions are observed for all the collision gases except helium, and vary with the chemical nature of the collision gas. As

indicated above, association product ions are probably
not formed in MIKES instruments, and collision gas ions
due to charge exchange that may be formed are undetected.
Furthermore, the relative intensities of fragment ions in
MIKES spectra do not vary when the collision gas is
changed (20). This result would be expected for the high
energy electronic excitation process described earlier.

The effect of changing the collision gas on the low-
energy CID of CH_4^+ is illustrated in Figure 2-2. In
these experiments the noble gases from helium to xenon,
plus nitrogen, were all studied, each at the same pres-
sure, approximately 10^{-3} torr, with an ion axial energy
of 10 eV. In Figure 2-2 the intensity of each fragment
ion (F_i) of CH_4^+ (P) relative to the total ion signal
$(\Sigma F_i + P)$ is plotted against the energy lost in each frag-
mentation. The energy loss values are taken from an
earlier MIKES study (21). The fragment ion intensities
increase for collision with the noble gases from He to Xe,
with N_2 falling between Ar and Kr. The relative intensity
of the C^+ and CH^+ fragments compared to CH_2^+ and CH_3^+
also increases from He to Xe. The degree of fragmentation
appears to be related to either collision gas mass or size.
Figure 2-3 shows the relative intensity of each ion plotted
against the square of the collision gas diameter. Experi-
mental conditions are the same as for Figure 2-2. The
data points for each fragment ion are reasonably smooth
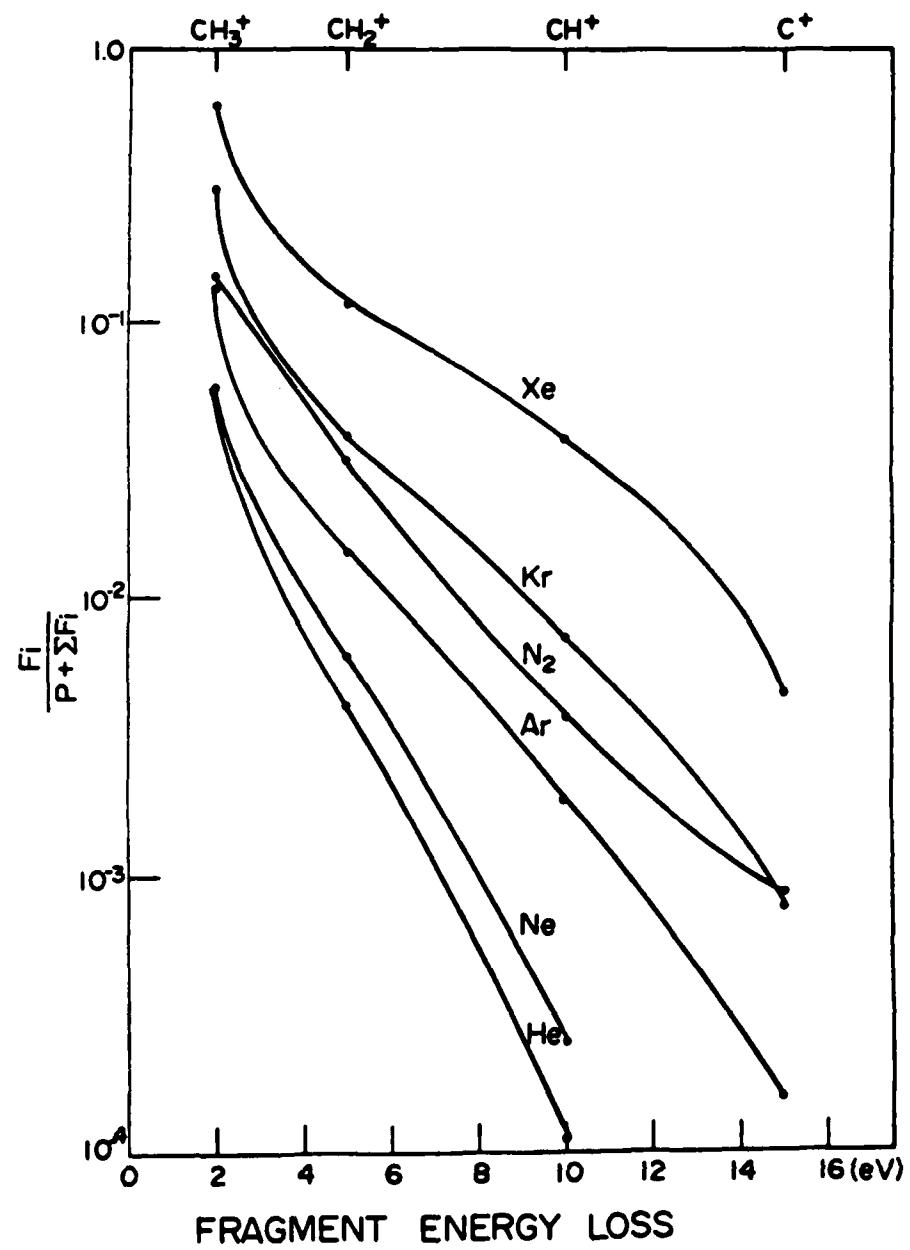
Figure 2-2. Effect of collision gas identity on the fragmentation of CH_4^+.
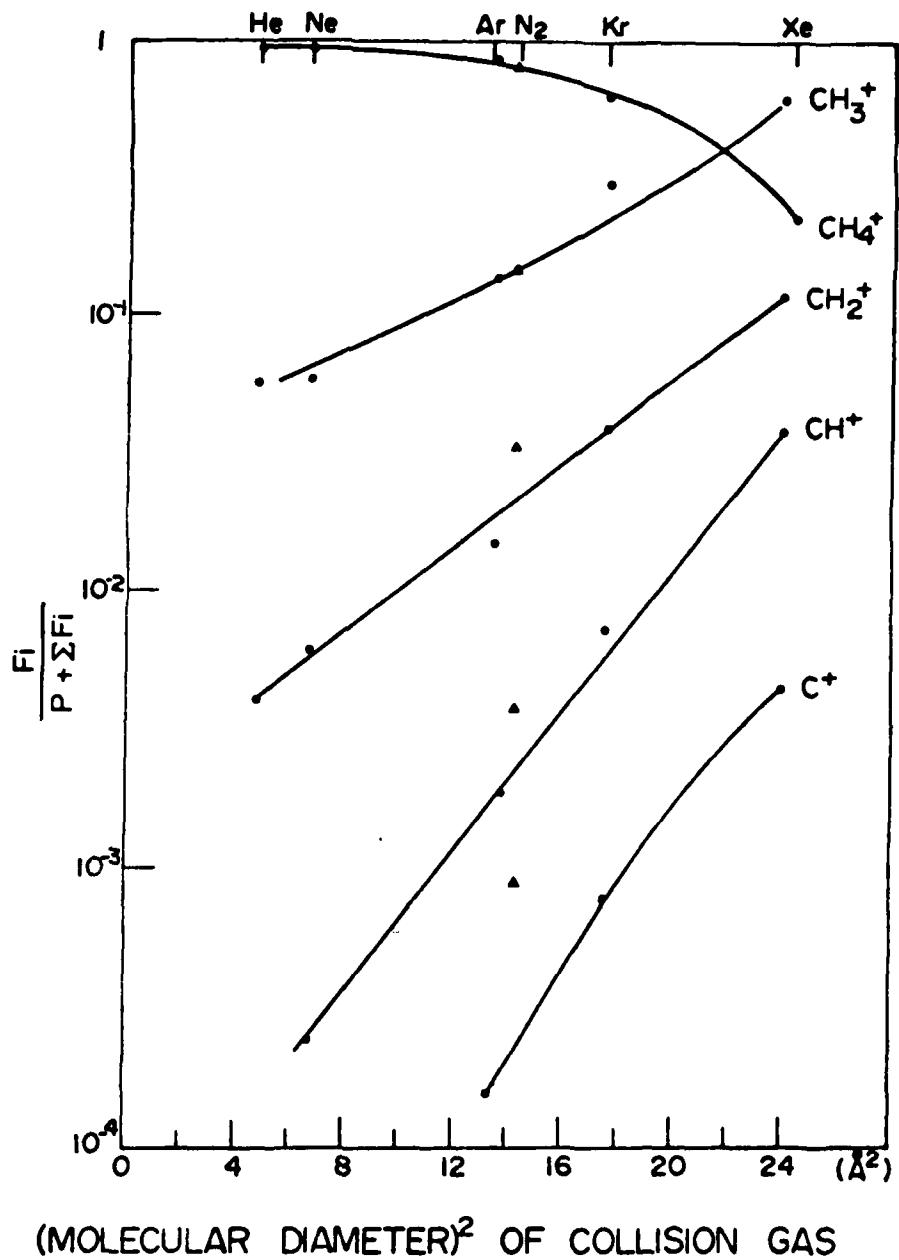
Figure 2-3. Relative intensity of $CH_4^+(P)$ and its fragments (F_i) as a function of the square of the collision gas diameter.

and linear except for the points corresponding to the N_2 collision gas, which lie above the line for C^{+}, CH^{+}, and CH_2^{+}. The diatomic N_2 molecule is more efficient for fragmentation than would be a noble gas molecule of the same diameter.

As mentioned above, in most MIKES studies it has been found that the collision gas identity has little effect on the appearance of the CID spectrum, although helium is often cited as more efficient for fragmentation than heavier collision gases (20). Recently, however, Cooks has obtained data which indicate that heavier collision gases are more efficient at both fragmenting and scattering ions (22). The fact that, in some experimental configurations, the lighter collision gases show higher overall CID efficiencies indicates that the fragmentation efficiency does not increase as rapidly as does the scattering loss as the collision gas size is increased.

Collision Gas Pressure

The effect of collision gas pressure on the fragmentation process is discussed in Chapter 5. In that chapter, Figure 5-4 shows the effect of increasing N_2 collision gas pressure on the fragmentation of CH_4^{+}. Several effects are observed. As the pressure is increased, the number

of ions undergoing collision (and therefore the frag-
mentation efficiency) is increased; at higher pressures
multiple collisions become important, increasing further
the fragmentation efficiency. As the pressure is increased,
however, the collection efficiency drops due to increased
scattering. The overall CID efficiency exhibits a maximum
at some intermediate pressure dependent on the collision
gas and ions involved.

Ion Kinetic Energy

Finally the effect of ion kinetic energy on the frag-
mentation process has been studied. The ion kinetic energy
is composed of two components, the axial energy from the
accelerating potential between the quadrupole common and
the ion source, and the transverse energy from the quadru-
pole RF field.

The effect of ion axial energy on the fragmentation
of CH_4^+ is shown in Figure 2-4. The argon collision gas
is at a pressure high enough (10^{-3} torr) for multiple col-
lisions to occur. The formation of CH_3^+ is nearly inde-
pendent of axial energy, but loss of 2,3, and 4 hydrogens
shows increasing axial energy dependence, with a maximum
C^+ production (which requires approximately 15 eV (21))
at about 15 eV. At lower axial energies, the path followed
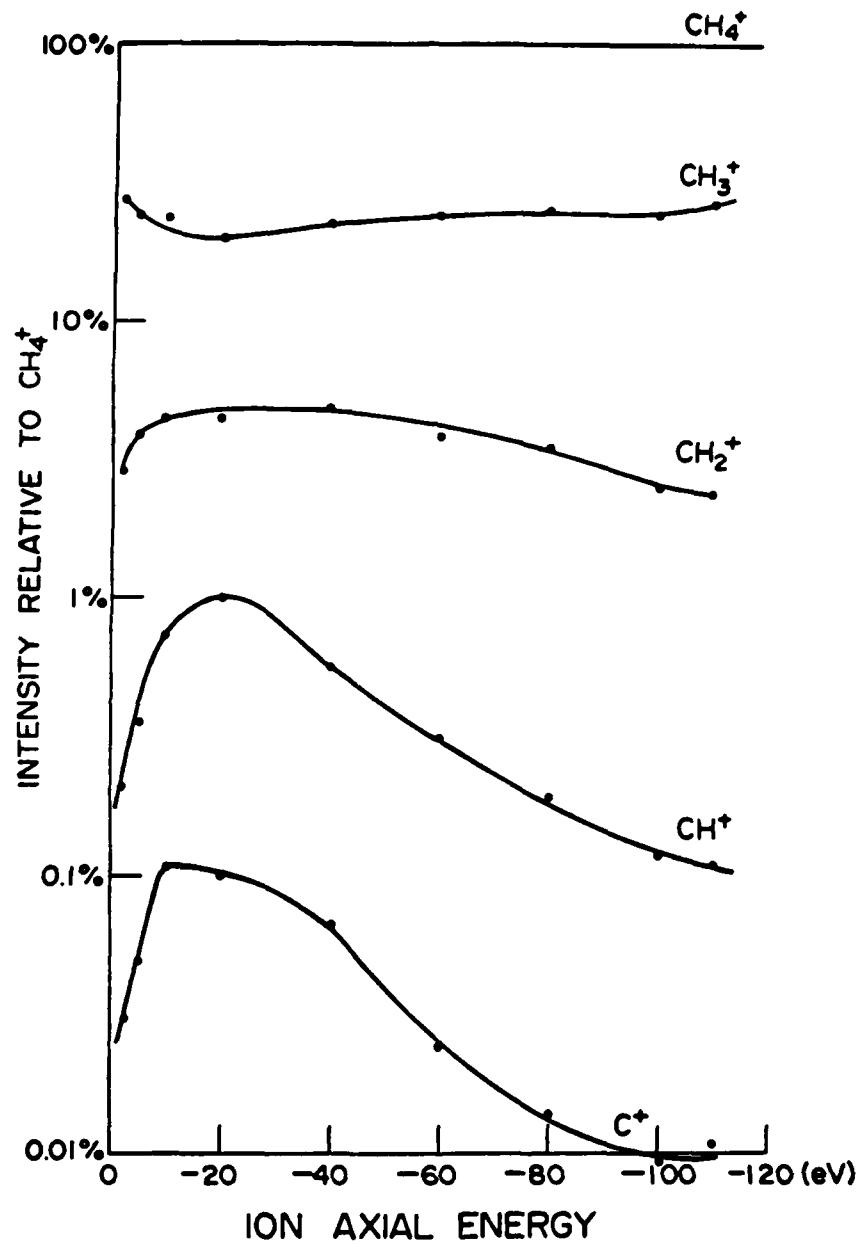
Figure 2-4. Effect of ion axial energy on the relative
intensity of the fragments of CH_4^+.

by the ions is longer due to more orbits in the RF field, and hence more collisions (of lower energy) occur. As the axial energy is increased, the fragmentation efficiency increases to a maximum, and then decreases as the cross section for momentum transfer drops, as observed in other momentum transfer reactions (17). Initially, an increase in axial energy increases the amount of energy available for vibrational excitation. It can be visualized that at higher kinetic energies (greater relative velocities), the ion and gas molecule do not "stick" together long enough for significant vibrational excitation to take place.

The ions may pick up transverse kinetic energy from the RF field in the center quadrupole. From digital simulations published earlier of the ion trajectories in the RF field, an average transverse energy of a few eV is indicated (2). Furthermore, the simulations indicate that the transverse energy is independent of both the peak RF voltage and the RF frequency. Experimental data confirm that the RF voltage over a range from 0 to 720 VpRF has no effect on the fragmentation process (2).

The total ion kinetic energy is the sum of the transverse and axial energies, and is typically 10-15 eV. The fragmentation process occurs, therefore, by a very efficient conversion of a portion of the ion's kinetic energy into internal energy. From these experiments it appears that the low-energy collision process in the center quadrupole

can involve a significant transfer of momentum. Further-
more, the ion-molecule interaction can last long enough
for a collision complex to form, and a variety of col-
lision products, including association products, to result.
The characterization of the collision process is a con-
tinuing project, with special emphasis on the energy transfer
process. Included are experiments to determine the effect
of collision gas parameters such as polarity and chemical
reactivity, and studies of isotopic scrambling to elucidate
the nature of the collision complex.

CHAPTER 3

MIXTURE ANALYSIS

Commercial mass spectrometers were developed in the 1950's to analyze the complex mixtures encountered in petroleum production. The difficulties involved in the analysis of the resultant spectra led to the increased use of chromatographic methods, at the expense of mass spectral techniques. The eventual combination of mass spectral analysis with gas chromatography (GC/MS) has produced one of the most powerful and widely accepted analytical methods (5). Interest in alternate techniques has remained active, however, due to the limitations on the thermal stability and volatility of samples, and the time-consuming nature of GC. Although difficult to interface to MS, liquid chromatography (LC) has generated considerable interest in recent years as a prior separation technique (6). While LC reduces the problems associated with involatile and thermally labile samples, it does not significantly increase the speed of separation. This chapter describes the use of mass spectrometry for both separation and identification of mixture components (MS/MS). While MS/MS has been implemented using MIKES instruments (23,24), this is the first application of tandem quadrupoles to mixture analysis.

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Mixture Analysis Technique

The molecular ions for all the components of a mixture
can be produced by a soft ionization technique (e.g.,
chemical ionization) which results in very little frag-
mentation, and can then be separated by the first mass
filter. The molecular ion for one component at a time
can be selected with the first quadrupole, fragmented in
the second, and the third scanned to obtain the result-
ing mass spectrum. The selectivity and discrimination
which result from the use of two stages of mass separation
can often improve the detection limit of the mass spec-
trometric technique due to the elimination of chemical
noise (23).

The use of mass spectral separation of the components
of a mixture in MS/MS eliminates the time delays as-
sociated with the chromatographic separation used in GC/MS
and LC/MS. Because all the components are available at
any time and in any order, only those components of par-
ticular interest need be analyzed. Each component may be
selected for as much or as little time as is required to
determine its identity and its quantity. Continuous analysis
of a sample is possible in such applications as atmospheric
analysis without the time delays associated with batch
sampling for chromatographic analysis. The limitations of
GC/MS regarding involatile and thermally labile samples

are largely eliminated by the MS/MS technique. Direct
insertion probes and field desorption or chemical desorp-
tion could be used to introduce samples which are not
amenable to GC separation.

The triple quadrupole mass spectrometer is especially
versatile for mixture analysis due to the availability of
the different operational modes described in Chapter 5.
A spectrum of all the ions produced by soft ionization of
the sample may be obtained by scanning the first quadru-
pole with the second and third in RF-only (total ion)
mode. The ions may then be selected by the first quadru-
pole, fragmented, and their mass spectra obtained by scan-
ning the third quadrupole. If specific compounds which
produce known fragment ions are to be detected, then mul-
tiple reaction monitoring may be employed. In this tech-
nique, selected parent ion/daughter ion pairs are sequen-
tially selected by the first and third quadrupoles. Those
components which contain a specific functional group may
be rapidly identified if that functionality produces a
characteristic fragment ion, and the third quadrupole is
set to that ion while the first quadrupole is scanned.
If instead, a characteristic neutral loss is being sought,
the first and third quadrupoles may be scanned with a fixed
difference in mass.

Application Examples

Our first publication (1) contained an example of mixture analysis performed on the triple quadrupole mass spectrometer at La Trobe University (see Appendix A). In this study a mixture of cyclohexane and three minor components (benzene, n-hexane, and cyclohexanone, each present as 5% of the mixture), was analyzed. The spectrum of each mixture component was reproducible and showed good agreement with the spectrum of the pure compound.

An example of the improvement in detection limit that can result from the elimination of chemical noise appears in Chapter 5. In this case a sample of 10 ppm CH_4 in N_2 was analyzed by monitoring the $CH_4^+ \rightarrow CH_3^+$ reaction. A detection limit of 20 femtograms was determined, a hundred-fold improvement over the detection limit obtained by simply monitoring the CH_4^+ , CH_3^+, or CH_2^+ ions directly. This improvement results from the elimination of chemical noise caused by the interference of $^{14}N^+$, $^{15}N^+$ and residual O^+ ions.

As a third example of mixture analysis, the following sample containing five components at equal concentration was chosen: two isomers of molecular weight 114, 3-heptanone and n-heptanal; a compound isobaric with the other two at 114, n-octane; plus cyclohexane (84) and 2-pentanone (86). The mixture was ionized by 70 eV EI, although CI

would have simplified the mass spectrum. The CID spectra of the 114^+ ion from the individual components show unique fragmentation: 99^+ (M-15) for 3-heptanone, 96^+ (M-18) for n-heptanal, and 70^+ (C_5H_{10}) for n-octane. In the CID spectrum of the 114^+ ion in the mixture, it is possible to detect the individual components despite their being isomeric or isobaric. Figure 3-1 shows the CID spectrum of the 114^+ ion in the mixture as well as the reference CID spectra of 114^+ from the three pure compounds. The two isomers in the mixture may be identified with even greater confidence by obtaining the CID spectra of fragment ions in the EI spectrum of the mixture that are unique to the specific components. The CID spectra of 99^+ and 81^+ from the mixture exactly match the spectra of the fragments 99^+ from pure 3-heptanone and 81^+ from n-heptanal, respectively. The other two components are easier to identify in the mixture; the CID spectra of pure cyclohexane (84^+) and 2-pentanone (86^+) are nearly perfect matches with the CID spectra of these ions from the mixture. The CID spectra obtained for 84^+ and 81^+ from the mixture are compared with reference spectra in Figure 3-1.

A sixth and unexpected component was discovered in the mixture as well. The electron impact spectrum showed peaks at 120^+ and 105^+ which could not be attributed to any of the five known components. The CID spectra showed
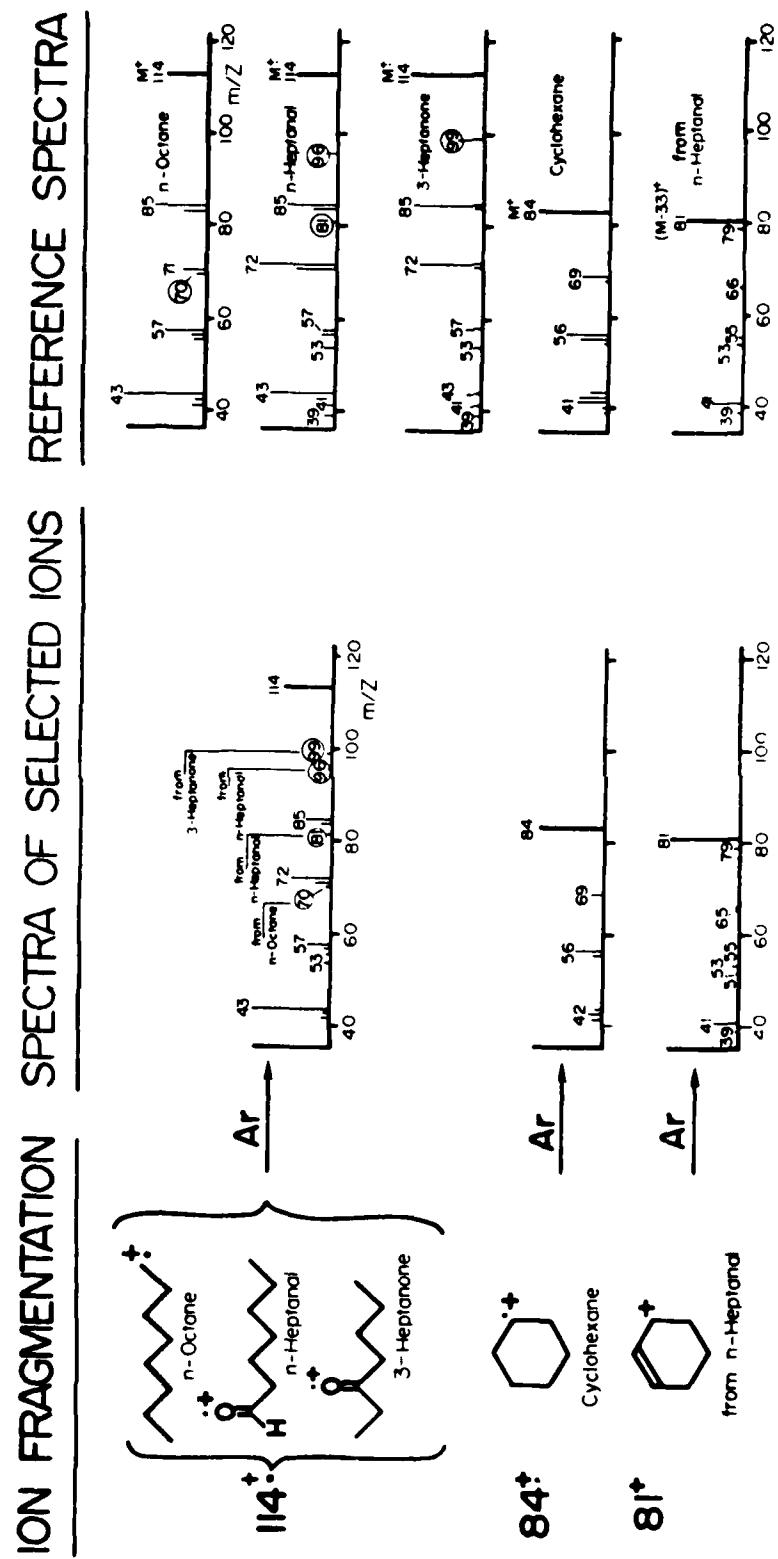
Figure 3-1. Comparison of CID spectra of selected ions in the EI spectrum of a five component mixture with reference CID spectra from pure components.

fragments from 120^+ at 105^+, 43^+, and 77^+ and fragments from 105^+ at 77^+, 51^+ and 26^+. Interpretation of these data suggested acetophenone as the impurity, and comparison with the reference CID spectra of acetophenone confirmed this. Careful study of the EI spectra of the pure components showed that the acetophenone was present as an impurity in the n-heptanal. A single standard addition experiment indicated an acetophenone concentration of approximately 5 parts per thousand. This gives an impurity concentration of 1 part per thousand in the mixture. These results demonstrate the ability of the triple quadrupole system to identify mixture components, including both isomers and isobaric compounds.

Conclusions

The technique of direct analysis of mixtures by triple quadrupole MS/MS has been developed, and it may eventually join GC/MS in widespread usage. The simplicity and versatility of the technique, combined with its ability to eliminate chemical noise, makes it a powerful alternative to current GC/MS and LC/MS methodology.

CHAPTER 4

STRUCTURE ELUCIDATION

An added dimension for structure elucidation is pro-
vided by selected ion fragmentation, in which several ion
species are generated from a sample, ions of a particular
mass are selected for fragmentation, and the resulting
fragment ions are mass analyzed. The use of two sequen-
tial stages of mass analysis with fragmentation occurring
between them makes it possible to determine the routes
of formation and fragmentation of ions in the mass
spectrum. A familiar example is the analysis of the
metastable peaks observed in the mass spectrum to show
parent/daughter relationships for some of the ions. A
more systematic technique for determining fragmentation
pathways is the combination of collision-induced dissocia-
tion (CID) with Mass-Analyzed Ion Kinetic Energy Spec-
trometry (MIKES) (25).

We recently introduced the concept of performing
selected ion fragmentation with a triple quadrupole mass
spectrometer (1). The use of tandem quadrupole mass
filters for mass analysis and the high efficiency of the
low-energy CID process when performed in a center quadru-
pole provides an extremely sensitive technique for the

direct and systematic analysis of fragmentation pathways.
The kinds of additional analytical information available
and its interpretation for elucidation of structure are
discussed in the sections that follow, and the chapter
concludes with a thorough analysis of the fragmentation
of nonan-4-one.

Data Available Through Selected Ion Fragmentation

The use of two stages of mass analysis in tandem makes
possible the identification of the formation and frag-
mentation pathways for every ion in a compound's mass
spectrum. If no collision gas is present, the unimolecu-
lar fragmentations observed correspond to the metastable
ions often observed in normal mass spectra. These transi-
tions can provide some information on the genetic relation-
ship of some few ions in the spectrum. Introduction of a
collision gas adds energy to the ions and increases both
the number and intensity of fragmentations that can be
observed. The ions produced by low-energy CID are less
likely to show isomerization or rearrangements than are
metastable ions, which have higher internal energies from
the source (25). Most of the ions observed in the low-
energy CID spectrum arise from simple cleavages and thus
provide useful data on the structures of the original
molecule.

As an example of the amount of data provided about a compound by selected ion fragmentation, consider the results for isopropanol. The electron impact mass spectrum of 1-propanol indicates 33 fragment ions, but gives no information about their formation or fragmentation. McLafferty catalogs 9 metastable ions observed for 1-propanol (26). Calculation of possible parent/daughter ion pairs from the metastable data indicates 8 confirmed fragmentations and one set of two possible transitions which could correspond to the ninth peak. We have measured the CID spectra of all 34 ions in the EI spectrum of 1-propanol and have observed 201 different fragmentations. The added dimension of information provided by knowing the formation and fragmentation of all the fragment ions of the compound makes this low-energy CID data extremely valuable for elucidation of structure.

The interpretation of the CID data can provide a number of different types of structural information about the sample. Consider the modes of operation of the triple quadrupole system: 1) By scanning the third quadrupole with the first set to pass a specific m/z ion, a spectrum of all the fragments which arise from the selected parent ion is obtained. 2) By scanning the first quadrupole with the third set for a specific ion, all the parent ions which can fragment to form that daughter ion are observed. 3) All the ions which lose a selected neutral

mass (<u>e.g.</u>, H_2O or $CH_3 \cdot$) are monitored by scanning both mass filters with a fixed mass difference between them.

The object of the interpretation effort is the assignment of structure to the major fragment ions and ultimately to the molecular ion. The interpretation techniques normally applied to EI mass spectra are quite useful for CID spectra since CID produces spectra qualitatively similar to those provided by EI. Most of the CID spectra obtained, however, are for even-electron fragment ions, whereas mass spectroscopists are most familiar with the fragmentation of odd-electron (<u>e.g.</u>, molecular) ions. Another very powerful approach to determining the structure of specific fragment ions is comparison of their CID spectra with a library of reference CID spectra of fragment ions of known structure. In contrast to library matching of EI spectra, which requires a library of enormous numbers of reference spectra, the library of reference spectra for identification of fragment ions requires relatively few entries.

As an example of the interpretation of CID data to answer a specific structural question, consider again the structure elucidation of i-propanol, $(CH_3)_2CHOH$. Another possible compound that could give the observed EI spectrum is acetic acid, CH_3COOH. In order to eliminate acetic acid as a possibility, consider the CID spectrum of $(M-CH_3)^+$ at m/z 45. The CID spectrum of 45 includes peaks at 44^+, 43^+, 42^+, and 41^+ which indicate the presence of at least

4 hydrogens in the fragment. This eliminates $COOH^+$ as
the structure of 45^+ and eliminates acetic acid as the
compound.

The selected ion fragmentation technique is carried
to its ultimate when all the fragmentation steps for a
compound are completely elucidated. The 201 fragmentations
observed for 1-propanol provide a dramatic indication
of the amount of structural information made available by
selected ion fragmentation.

Selected Ion Fragmentation Instrumentation

The tandem mass spectrometer makes possible the mass
analysis of the fragment ions of mass-selected parent ions.
Two quadrupoles in tandem have been employed to study ion-
molecule reactions (11), and triple quadrupole systems have
been applied to study the photodissociation of ions (12,13).

The triple quadrupole mass spectrometer used in this
study has been described (27). It consists of, in series,
a dual chemical ionization/electron impact (CI/EI) ioniza-
tion source, a quadrupole mass filter, an RF-only quadrupole
that can be pressurized for CID, a second quadrupole mass
filter, and an electron multiplier. Mass resolution of
one part in 1500 is possible over the entire mass range of
1-1000 amu. The high efficiency of each component in the
system makes detection limits in the femtomole range

possible by monitoring specific fragmentations (27).

Prior to the development of the triple quadrupole mass spectrometer, all selected ion fragmentation for analytical purposes had involved the use of double-focusing mass spectrometers to determine fragmentations (either metastable on collision-induced dissociations) which occur either between the sectors or before the first sector. For a double-focusing spectrometer with the electric sector preceding the magnetic sector, the technique is called Ion Kinetic Energy Spectrometry (IKES) if the electronic sector voltage is scanned, and high voltage (HV) scanning if the accelerating voltage is scanned. For a spectrometer in which the magnetic sector precedes the electric sector, the technique is called MIKES. All three techniques display peaks that are broadened by kinetic energy loss upon fragmentation, which makes it difficult to achieve unit mass resolution. The HV technique has the additional disadvantage of a limited range of fragment mass (neutral loss less than half the parent mass). Nevertheless, both IKES and MIKES have been proven to be powerful techniques for structure elucidation (25,28-31).

The Fragmentation of Nonan-4-one

The electron-impact induced fragmentation of aliphatic ketones has been widely investigated (32). A number of specialized techniques have been utilized to help in these studies, including metastable decomposition studies (33-35), ion cyclotron resonance (ICR) (36), and the use of deuterium labelled compounds (35-38). Nonan-4-one has received particular attention, including a study of the metastable ions observed from this compound with an Ion Kinetic Energy (IKE) Spectrometer (38). We have performed a detailed study of the fragmentation of this compound using low-energy collision-induced dissociation (CID) of selected ions in a triple quadrupole mass spectrometer.

Figure 4-1 displays all the collisional fragmentations observed in this study (below the diagonal) and all the metastable transitions seen in the IKES study (above the diagonal) (38). The EI mass spectrum of nonan-4-one shows 47 fragment ions, and the metastable study indicates 37 confirmed and 7 unconfirmed metastable transitions. The triple quadrupole system shows over 400 CID peaks, which include the 44 fragmentations observed in the metastable data as well as a host of others. Not only does the triple quadrupole system with CID produce a significant increase in the number of fragmentations observed, it also provides direct mass analysis of both the parent and
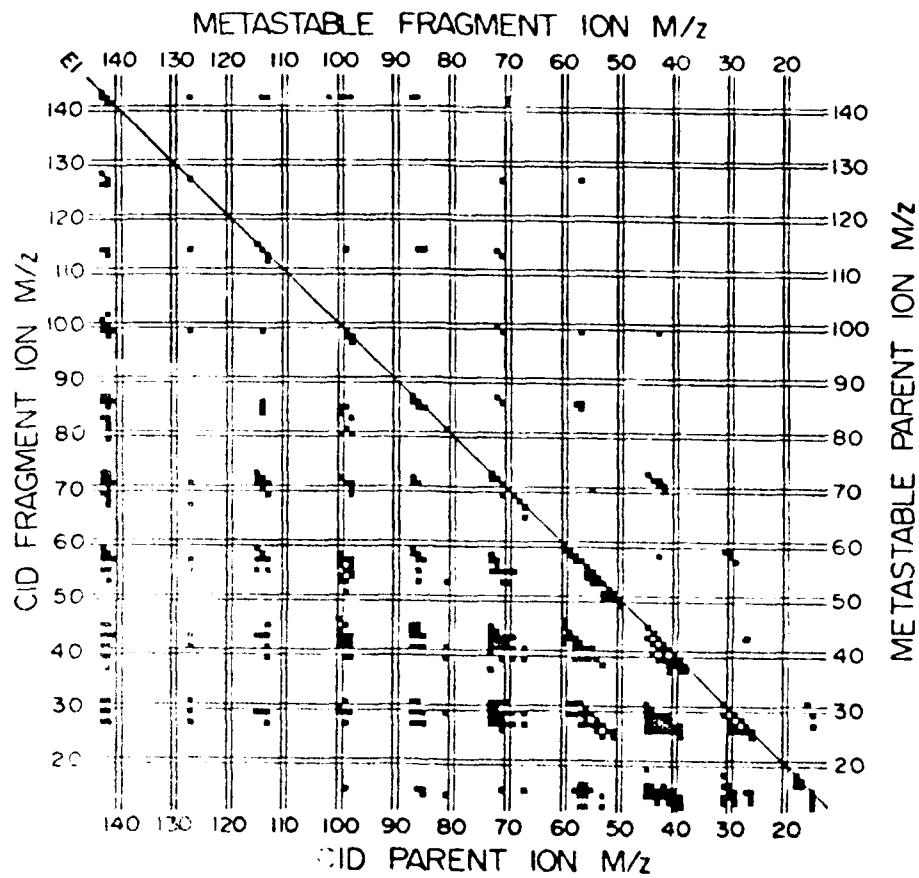
Figure 4-1. Collision-induced fragmentations of nonan-4-one from this study (below the diagonal), metastable fragmentations from previous IKES study (36) (above the diagonal), and EI mass spectrum (along the diagonal).

daughter ions at unit mass resolution.

A combination of complementary methods was used in the IKES study of metastable transitions (38). The kinetic energy loss upon metastable fragmentation results in broad peaks which make difficult unambiguous mass assignment of the parent and fragment ions (e.g., $142^+ \rightarrow 99^+$ or $142^+ \rightarrow 98^+$) in IKES scans. (In these scans it is the ratio of parent ion mass/charge squared to daughter ion mass/charge that is actually measured, so that several pairs of parent/daughter ions (e.g., $142^+ \rightarrow 86^+$ and $71^+ \rightarrow 43^+$) may contribute to a single peak). Comparison of IKE spectra of isotopically labelled and unlabelled samples can help in the assignment of specific transitions for each peak. In the high voltage scanning technique that was also employed, mass losses of greater than 50% cannot be observed.

The major fragmentations observed in the CID studies are depicted in Figure 4-2. The stars indicate transitions that are also observed in the metastable studies (38). Redundant pathways are not shown (e.g., $142^+ \rightarrow 85^+$ is not shown since the transitions $142^+ \rightarrow 114^+$ and $114^+ \rightarrow 85^+$ do appear). Note that the CID data do not indicate any ions of m/z not seen in the EI mass spectrum; rather, they provide interconnections between these ions, specific fragmentation pathways for the production and further fragmentation of each ion.

The fragmentations normally attributed to alkanones
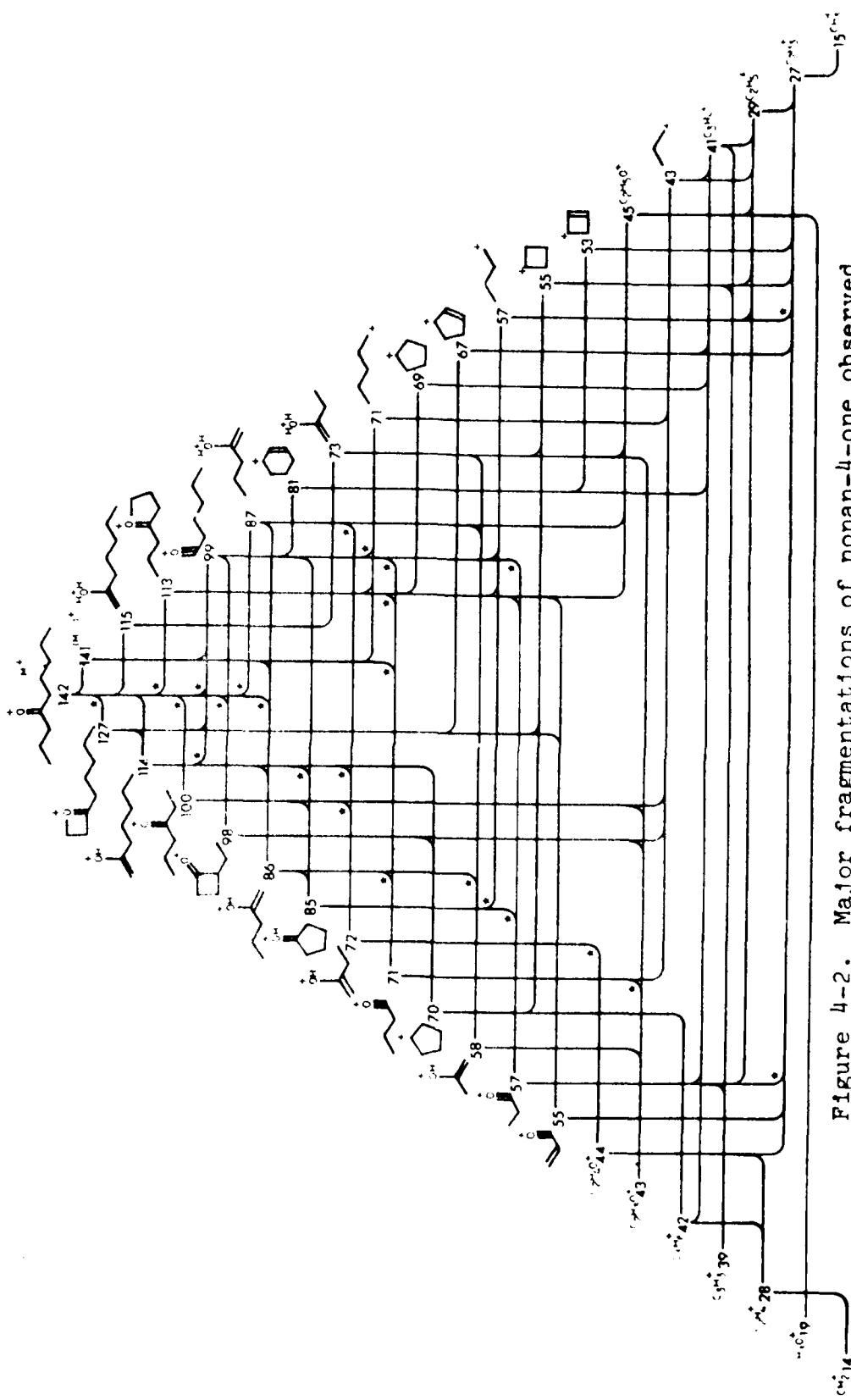
Figure 4-2. Major fragmentations of nonan-4-one observed in this CID study. Starred transitions have also been observed in previous metastable studies (38).

are all observed, including α-cleavage ($142^+ \rightarrow 99^+$ and $142^+ \rightarrow 71^+$), loss of CO or C_2H_4 from the α-cleavage ions ($99^+ \rightarrow 71^+$ and $71^+ \rightarrow 43^+$), McLafferty rearrangement in the long chain ($142^+ \rightarrow 86^+$), and the resultant double Mc-Lafferty rearrangement ($86^+ \rightarrow 58^+$). These transitions, also seen in the IKES study of metastables, account for the genesis of the five major fragment ions in the electron impact mass spectrum. These fragmentations also shed some light on the preferential α-cleavage of the short or long chain. At high collision gas pressures (1×10^{-4} torr), the long chain is preferentially eliminated, as is the case in 70 eV EI spectra (32). At lower collision gas pressure (2×10^{-5} torr), however, the short chain is preferentially lost, a feature that is also observed in 10 eV EI spectra (39) and metastable studies (33). It has been postulated (39) that further decomposition of the ion resulting from α-cleavage of the short chain is the cause of its reduced intensity in the 70 eV EI spectrum. Further fragmentations are minimized at 10 eV, and therefore the short chain α-cleavage ion remains the more intense. The CID data are in agreement with this rationalization, since multiple collisions and therefore further fragmentations are more likely at higher collision gas pressure. This rationale requires faster rates of decomposition and/or more pathways for the further decomposition of the ion which results from α-cleavage of the short

chain compared to that from the long chain loss. That reasoning can be checked by comparing the degree of fragmentation in the CID spectra of the two α-cleavage ions. The ion arising from α-cleavage of the short chain (99^+) shows 97% fragmentation (only 3% of the ion current is due to 99^+) at 1×10^{-4} torr compared to only 88% fragmentation for 71^+, the ion arising from the α-cleavage of the long chain. This higher probability for further fragmentation of 99^+ compared to 71^+ explains why 71^+ predominates in cases where enough energy is available for further fragmentation (70 eV EI or high pressure CID) and why 99^+ is larger when further fragmentation is unlikely (low energy EI or low pressure CID).

In addition to these fragmentations already observed, a number of new transitions not previously reported are observed, such as the McLafferty rearrangement in the short chain and its further fragmentation $(142^+ \rightarrow 114^+, 114^+ \rightarrow 86^+, 114^+ \rightarrow 70^+, 114^+ \rightarrow 58^+)$, eleven fragmentations of the methyl-loss ion (127^+) which confirm the methyl loss in the short chain, the formation and fragmentation of the hydrogen-loss ion $(142^+ \rightarrow 141^+$ and $141^+ \rightarrow 99^+, 141^+ \rightarrow 86^+)$, the loss of water from the α-cleavage ions $(99^+ \rightarrow 81^+, 71^+ \rightarrow 53^+, 57^+ \rightarrow 39^+)$ and the fragmentation of the resultant hydrocarbon ions. Over 350 fragmentations not previously reported are shown in Figure 4-1. A number of these are discussed in the sections which follow, together

with fragmentations which confirm or contrast with those reported by the IKES study. Discussion of the formation and fragmentation of specific ions appears in the following sections, arranged in order of decreasing m/z. All the transitions discussed can be seen in Figure 4-?.

Group A; 142^+, 141^+

The CID spectrum of 142^+ is very similar in appearance to the EI spectrum of the molecule. The same fragments are observed, with the exception of the isotopic peaks, which are eliminated by the selection of 142^+. By controlling the collision gas pressure and ion kinetic energy, the relative intensity of the fragment peaks in the CID spectrum can be made to agree almost exactly with that in the normal EI spectrum. The $142^+ \rightarrow 141^+$ transition, not seen in the metastable study, is observed in the CID data.

Group B; 127^+

The CID data confirm that the $142^+ \rightarrow 127^+$ transition is due to $CH_3\cdot$ loss from the short chain, as previously indicated by deuterium labelling in the metastable study. Major CID fragments of 127^+ are due to further loss in the short chain to produce 114^+ and 99^+, indicating that the long chain in 127^+ is still intact. Another

fragmentation is the loss of the elements of propanol to form 67^+, $C_5H_7^+$.

Group C; 113^+-115^+

The fragmentation of 113^+ indicates that it is formed by loss of $C_2H_5\cdot$, probably from the long chain of the molecular ion, since both 99^+ and 86^+ are missing. Note also the loss of C_2H_4O to form $C_5H_9^+$.

The authors of the metastable study assigned the weak $142^+ \rightarrow 114^+$ metastable to the fragmentation process in Equation (1), based on deuterium labelling.

$$142^+ \xrightarrow{-C_2H_4} 114^+ \qquad (1)$$
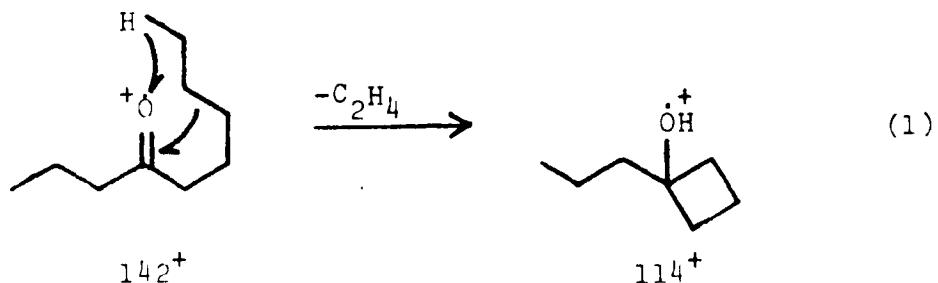
All fragmentations of the 114^+ ion, however, were attributed to the ion which arises from the McLafferty rearrangement in the short chain as shown in Equation (2).

$$142^+ \xrightarrow{-C_2H_4} 114^+ \qquad (2)$$
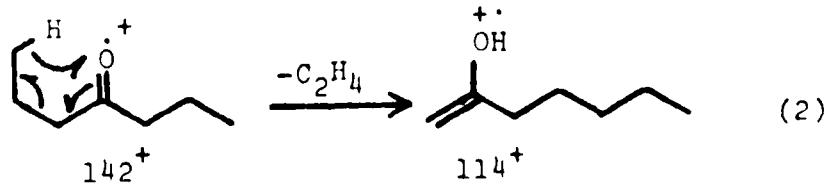
Based on the intense fragment ions of 114^+ observed at 57^+ and 58^+ in this study, the structure of the 114^+ ion produced by electron impact is that shown in Equation (2). It is quite possible that the McLafferty rearrangement which is observed in EI also occurs by CID.

The ion at 115^+ is not an isotopic counterpart of 114^+ since its fragmentation bears little resemblance to that of 114^+. The 55^+ fragment ion is approximately three times as intense as any other ion which could result from the following formation of 115^+ from a two-hydrogen rearrangement, loss of C_3H_6 to form 73^+, and loss of H_2O to form 55^+ [Equation (3)].

$$142^+ \quad \xrightarrow{-C_2H_3\cdot} \quad 115^+ \quad \xrightarrow{-C_3H_6} \quad 73^+ \quad (3)$$

$$\downarrow {-H_2O}$$

$$55^+$$
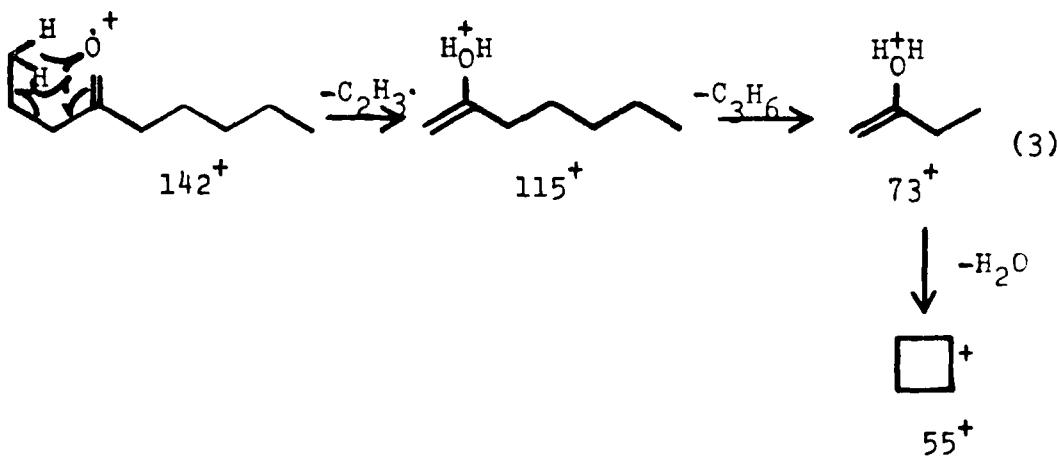
Group D: 98^+-100^+

In the study of metastable fragmentation, 99^+ was observed to be formed from 142^+ by α-cleavage of the short chain as well as from 114^+. The CID data show formation

of 99^+ from 141^+ and 127^+ as well. The fragmentation of 99^+ shows the expected losses, plus the unexpected loss of water to form 81^+, as shown in Equation (4).

$$(4)$$
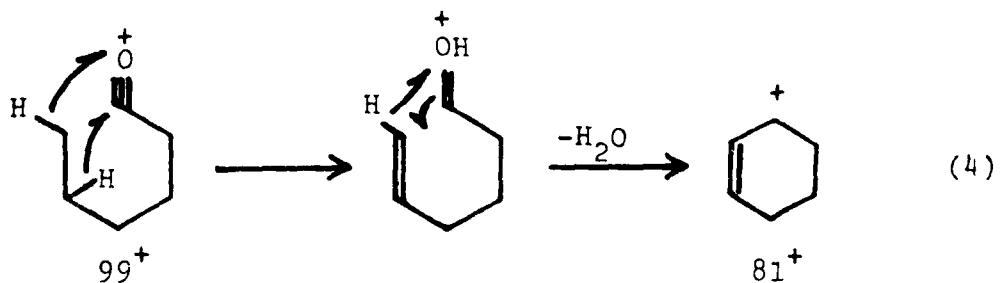
The mechanism of H_2O loss in branched-chain ketones has been elucidated (37), but the very low intensity of the ion due to this loss in straight-chain ketones has precluded its study by deuterium labelling or from experiments involving metastables. Despite the low intensity of the water-loss ion, the CID data make it possible to observe not only the loss of water, but also the further fragmentation of the product ion (81^+). Analogous fragmentations which indicate the loss of water are seen for the other α-cleavage ion (71^+), as well as for 73^+, 57^+, 45^+, 44^+, and 31^+.

The 98^+ ion is seen as a fragment of 142^+ in both the CID and metastable studies, with an intensity of approximately 5% of 99^+. The CID spectrum shows a moderately

intense $99^+ \rightarrow 98^+$ fragmentation, which suggests that the 98^+ may be formed by a two-step fragmentation from 142^+ through 99^+.

Group E; 81^+, 85^+-87^+

The 81^+ ion does not appear as part of any metastable transition with sufficient intensity to be observed in previous studies. In addition to its formation, as described in Group D above, its fragmentation is clearly observed. The ion series 53^+, $41^+/39^+$, 29^+, 14^+ from the even-electron ion suggests a 6-membered ring.

The formation of 85^+ from 142^+ and 114^+ was noted in metastable studies. We observe that it may also arise from the fragmentation of 100^+, 99^+ and 86^+. The 85^+ shows the ion series 57^+, $43^+/41^+$, $29^+/27^+$, $15^+/14^+$; the absence of a 71^+ or 70^+ peak is in agreement with the cyclo-pentanone structure.

The ion at m/z 86^+ is formed as expected by the Mc-Lafferty rearrangement in the long chain of the molecular ion. Another route for its formation, however, is by loss of C_2H_4 from the other McLafferty rearrangement ion, 114^+. The 87^+ ion is formed by the "McLafferty+1" rearrangement from the molecular ion. Its fragmentation is quite similar to that of 86^+ plus a hydrogen, with the exception of the very large $87^+ \rightarrow 45^+$ transition (loss of C_3H_6).

Group F; 67^+-73^+

The 67^+ ion has not been observed in earlier metastable studies. Its formation was discussed in Group B above. Its fragmentation pattern follows that expected for the even-electron $C_5H_7^+$ ion, and is analogous to the fragmentation of 81^+ and 53^+. The 69^+ and 70^+ ions also show fragmentation patterns indicative of cyclic alkane ions. The CID spectrum of the even-electron 69^+ shows very good agreement with that of 69^+ from cyclohexane; the odd-electron 70^+ ion shows very similar fragmentation to the 70^+ ion of n-octane.

Two ions are isobaric at 71^+, $C_5H_{11}^+$ and $C_4H_7O^+$. By careful deuterium labelling in the metastable studies, the 71^+ ion from 142^+, 141^+, 113^+, and 86^+ has been shown to be $C_4H_7O^+$; the 71^+ peak from 99^+ has been found to correspond to both $C_5H_{11}^+$ and $C_4H_7O^+$. In this CID study, the formation of 71^+ from all of these ions is observed, as well as the production of 71^+ from 127^+, 115^+, 114^+, 98^+ and 87^+. By consideration of other fragmentations and the neutral losses involved, it is possible to assign the $C_4H_7O^+$ structure for the 71^+ fragment of 87^+ (by $87^+ \rightarrow 86^+ \rightarrow 71^+$) and 98^+ (loss of 27). For the other three parent ions (127^+, 115^+, 114^+) it is not possible to confirm the structure of the 71^+ fragment based on the available data. Deuterium labelling would aid in these studies.

The fragmentation spectrum of 71^+ from the EI spectrum of nonan-4-one shows 43^+ as the most intense fragment, with other fragments at 27^+, 29^+, 31^+ (with intensities 0.40, 0.25 and 0.015, respectively, relative to 43^+), 15^+, 39^+, 41^+, 53^+, and 55^+. For comparison, the CID spectra of $C_4H_7O^+$ from 2-pentanone and $C_5H_{11}^+$ from n-octane were measured under similar experimental conditions. The $C_4H_7O^+$ ion shows the most intense fragment at 43^+, with other fragments at 27^+, 29^+, 31^+ (intensities 0.40, 0.08, and 0.075 relative to 43^+), 15^+, 39^+, 41^+, 45^+ and 53^+. The $C_5H_{11}^+$ ion produces a CID spectrum with 43^+ also the most intense fragment, and additional fragments at 27^+ and 29^+ (intensities 0.05 and 0.36 relative to 43^+), 15^+, 39^+, 41^+, 55^+, and 56^+. The 71^+ ion from nonan-4-one shows fragments corresponding to both the possible ions, and is therefore undoubtedly composed of both $C_4H_7O^+$ and $C_5H_{11}^+$. Based on the relative intensities of the 27^+ and 29^+ peaks, the contributions to the 71^+ ion signal are estimated to be 30% $C_5H_{11}^+$ and 70% $C_4H_7O^+$.

The 72^+ ion yields the fragmentations expected for the addition of H to 71^+. The major pathways for formation of 72^+ are "γ-cleavage + 1" from 114^+ and 87^+, and McLafferty rearrangement from 100^+. The formation of 73^+ from 115^+ and its fragmentation by loss of H_2O to form 55^+ was discussed in Group C. Other major fragmentation pathways for 73^+ are loss of C_2H_4 and C_2H_6 to form 45^+ and 43^+ respectively.

Group G: 50^+-60^+

The ions at 50^+, 51^+, 52^+, 53^+, and 54^+ all show fragmentation spectra that are quite similar to those for the same m/z ions from hydrocarbons such as cyclohexane and n-octane. The 55^+ ion, however, shows a peak in the CID spectrum at 27^+ that is 1/3 greater in relative intensity than the 27^+ ion seen from 55^+ ($C_4H_7^+$) in reference alkane CID spectra. This may indicate that a small portion of the 55^+ peak is due to the $C_3H_3O^+$ ion. Although the CID spectrum of $C_3H_3O^+$ has not been measured for reference, the major fragmentation would likely be $55^+ \rightarrow 27^+$, with loss of CO. In the EI mass spectrum of cyclopentanone, the $C_3H_3O^+$ ion comprises 94% of the 55^+ base peak, and its formation has been carefully studied (40). It is improbable or impossible that 55^+ formed from 142^+, 115^+, 113^+, 86^+, 73^+, 72^+, 71^+, ($C_5H_{11}^+$), 70^+ or 69^+ would be $C_3H_3O^+$, but it is possible that fragmentation of 127^+, 99^-, 98^+, and 71^+ ($C_4H_7O^+$) could produce $C_3H_3O^+$ as well as $C_4H_7^+$.

The peak at m/z 56^+ can also correspond to two different ions, $C_4H_8^{+\cdot}$ and $C_3H_4O^{+\cdot}$. The fragmentation matches that of $C_4H_8^{+\cdot}$ with the exception of the 28^+ ion which is more intense than in the reference spectrum. The extra intensity at 28^+ is undoubtedly due to the $C_2H_4^{+\cdot}$ fragment of $C_3H_4O^{+\cdot}$. Both $C_4H_9^+$ and $C_3H_5O^+$ are possible structures for the 57^+ ion. Only the 57^+ fragment from 85^+ has been assigned (as $C_3H_5O^+$) based on metastable

results. The CID data shows that the 86^+ ion also frag-
ments to form $C_3H_5O^+$, but it is impossible to positively
assign without further study either the $C_4H_9^+$ or $C_3H_3O^+$
structure to the other 11 fragmentations observed that
lead to 57^+. The CID spectrum of 57^+ from nonan-4-one
shows a peak at 31^+ that is not observed in the otherwise
similar spectrum of $C_4H_9^+$ from n-octane. The 31^+ ion
probably corresponds to the loss of C_2H_2 from $C_3H_5O^+$.

The CID spectrum of the 58^+ ion shows two major frag-
ments, 43^+, and 15^+. The interpretation of the CID
spectrum indicates the acetone ion $(CH_3)_2CO^{+\cdot}$; comparison
with reference spectra shows it to be identical with those
for $(CH_3)_2CO^{+\cdot}$ from acetone and 2-pentanone.

Group H; 38^+-45^+

The ions at 38^+, 39^+, 40^+, and 41^+ all show very good
agreement with alkane reference CID spectra. The ions at
42^+, 43^+, and 44^+, however, are mixtures of alkane and
ketone ions. The 42^+ ion shows an additional intense
fragment at 14^+ undoubtedly due to the formation of $CH_2^{+\cdot}$
from $CH_2CO^{+\cdot}$.

The reference CID spectra of the two possible 43^+ ions,
CH_3CO^+ and $C_3H_7^+$, include all the same ions; the major
difference is the ratio of the intensities of the 27^+ and
15^+ peaks: approximately 5:1 for $C_3H_7^+$, and 1:20 for CH_3CO^+.
The 43^+ peak from nonan-4-one shows fragments at 27^+ and

15^+ in the ratio 1:4. Based on these data, the 43^+ peak corresponds to 75% CH_3CO^+, the remainder being $C_3H_7^+$. The 43^+ peak is quite common in the CID spectra; all but 3 ions above m/z 57^+ show a 43^+ peak.

The CID spectrum of 44^+ shows the fragmentations that would be expected for CH_3CO^+ with one C^{13} or an extra H. The 45^+ ion includes H_3O^+ (loss of acetylene) as one of the most intense fragment ions in its CID spectrum.

Group I; $26^+ - 31^+$

The ions at 26^+, 27^+, 28^+, 29^+ and 30^+ all give CID spectra which agree well with the reference CID spectra for hydrocarbon ions. The 31^+ ion, however, must contain O, and indeed fragment ions are observed at 18^+ and $(31-18)^+$.

Conclusions

The triple quadrupole mass spectrometer provides a wealth of data that can be interpreted to provide a new dimension of information for structure elucidation. The formation and fragmentation pathways of specific ions can be obtained in order to determine ion structure. Starting with every fragment of a compound, every fragmentation pathway for the entire molecule can be determined.

The application of the triple quadrupole system to the collision-induced dissociation of the ions of nonan-4-one has identified over 400 fragmentation paths. This enormous increase in the amount of information available for the structure elucidation of the compound compared to that obtained by earlier IKES metastable studies is a result of several features of the triple quadrupole system: (1) The use of CID increases the number of fragmentations that occur, and their intensity. (2) The high sensitivity of the system makes it possible to study transitions of very low intensity. (3) The use of two stages of direct mass analysis eliminates any ambiguity in the identification of parent and daughter ion m/z. (4) There is no restriction on the neutral loss. (5) Unit mass resolution is achieved and is unaffected by the kinetic energy loss upon fragmentation.

Interpretation of the CID spectra has made it possible to assign specific structures to a number of the fragment ions of nonan-4-one. Confirmation of these structures can be achieved by comparison of the spectra with reference CID spectra of ions of known structure. In the case of fragment peaks which correspond to two isobaric ions, it is possible to estimate the contribution of each ion by comparison with the reference spectra, without resorting to the high resolution necessary to separate the isobaric ions. The ability to measure the

probability of further fragmentation for the fragment ions which arise from α-cleavage has made it possible to explain the apparent preference for α-cleavage in the long chain in 70 eV EI spectra and for α-cleavage in the short chain at 10 eV.

A potentially powerful system for structure elucidation of organic compounds should be realized by the combination of complete CID fragmentation data with computer programs which use heuristic or pattern recognition techniques for structure identification. The completeness of the CID fragmentation data and their ability to show relationships among the ions in the mass spectrum should make computer interpretation extremely powerful.

CHAPTER 5

INSTRUMENTATION

An added dimension of mass spectral information is
provided by selected ion fragmentation whereby several
ionic species are generated from a sample, ions of a
particular mass are selected for fragmentation, and the
resulting fragment ions are mass analyzed. We recently
introduced the concept of performing selected ion frag-
mentation with a triple quadrupole mass spectrometer (1).
In this system, the selected ion fragmentation process
can provide enhanced selectivity and discrimination over
normal mass spectrometry without loss of sensitivity.

There are several applications of mass spectrometry
which benefit greatly from the added information con-
tained in the fragmentation spectrum of each source ion.
These include the elucidation of organic structures and
the analysis of mixtures. In structure elucidation applica-
tions, any fragment ion in a compound's normal mass spec-
trum can be selected with the first mass analyzer. This
"parent" ion is further fragmented, and the mass spectrum
of the resulting daughter ions is determined by scanning
the second mass analyzer. A complete fragmentation map
may be obtained by recording the mass spectrum of each
fragment ion of a compound. Figure 5-1 is an example of such
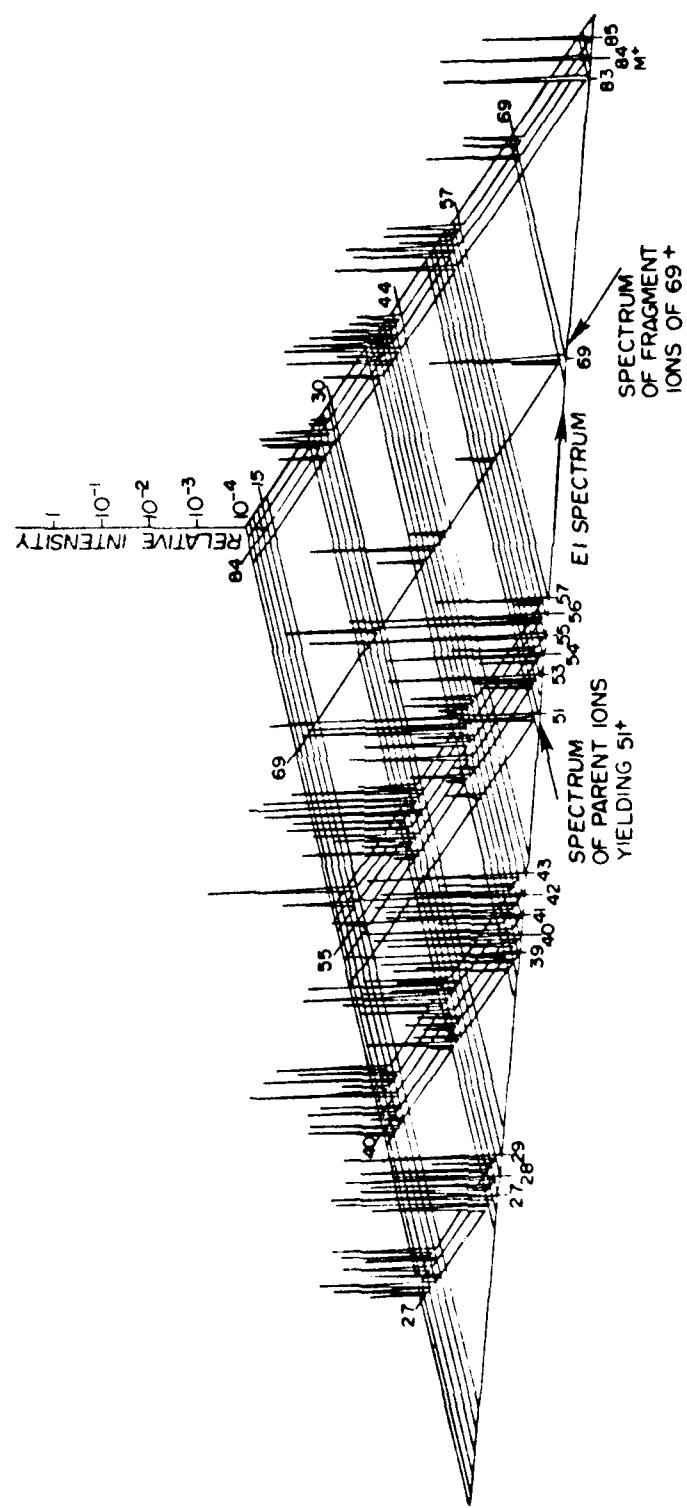
Figure 5-1.   Three-dimensional fragmentation map for cyclohexane.

a map, for cyclohexane. Note that the normal electron impact mass spectrum, displayed along the diagonal (fragment ion m/z=parent ion m/z), is the only information available without the added dimension of selected ion fragmentation.

For analysis of mixtures, the molecular ions for each component can be produced by soft ionization and then separated by the first mass analyzer. Thus, one component at a time, the molecular ion species can be selected, fragmented and the individual mass spectrum obtained by scanning the second analyzer. The added dimension in this case is the selectivity and discrimination achieved through mass separation of the molecular ions of the several components. The elimination of chemical noise that results can often improve the detection limit of the mass spectral technique (23).

The triple quadrupole mass spectrometer is a particularly simple and efficient approach to selected ion fragmentation. The ion fragmentation process is performed by collision-induced dissociation (CID) in an RF-only quadrupole which provides ion focusing and is highly efficient (2). The instrument consists of, in series, a dual chemical ionization/electron impact (CI/EI) ionization source, a quadrupole mass filter, an RF-only quadrupole that can be pressurized for CID, a second quadrupole mass filter and an electron multiplier, as shown in Figure 5-2. There are several possible modes of operation for the instrument:

(1) In order to obtain a normal mass spectrum (only
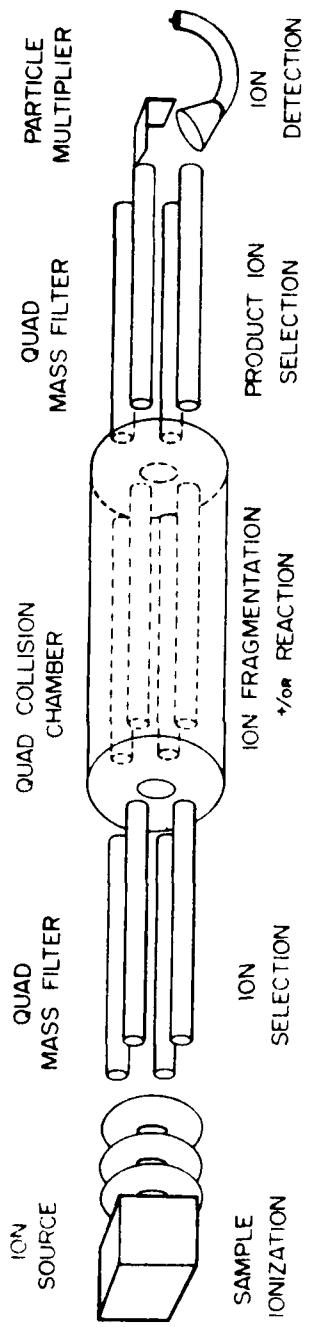
Figure 5-2. Conceptual diagram of the triple quadrupole mass spectrometer showing each component and its function.

one stage of mass analysis), the first mass filter is
scanned with the second and third quadrupoles in RF-only
(total ion) mode. The collision gas may be present or
not, since it does not significantly affect the number of
ions reaching the detector.

(2) A scan of the third quadrupole while the first
mass filter passes a specific mass produces a spectrum of
all the daughter ions from the selected parent ion. If
the collision gas is absent, the unimolecular decomposition
products (so-called "metastable" ions) will be measured.

(3) The spectrum of all parent ions that fragment to
produce a given daughter ion is observed by scanning the
first mass filter with the third quadrupole fixed on the
daughter ion mass.

(4) The observation of a specific neutral mass loss
is achieved by scanning both mass filters with a fixed
difference in mass. The use of a double focusing mass
spectrometer for neutral loss spectra has been suggested
recently as a complicated but useful technique for struc-
ture elucidation (41).

(5) A specific parent/daughter ion transition is
selected in single reaction monitoring (42), a technique
analogous to a single ion monitoring in gas chromatography/
mass spectrometry.

(6) The quadrupole's linear mass scale and fast
response permit rapid multiple reaction monitoring in

which multiple parent/daughter ion pairs are observed.

There are several other approaches to selected ion fragmentation, the most notable of which for analytical applications is Mass-Analyzed Ion Kinetic Energy Spectrometry, or MIKES (also called Collisional Activation Mass Spectrometry or CAMS, and Direct Analysis of Daughter Ions or DADI). This technique makes use of a double-focusing mass spectrometer in which the magnetic sector precedes the electrostatic analyzer. Fragmentation between the sectors can be unimolecular (metastable ions) or collisionally induced. MIKES has been demonstrated as a technique for selected ion fragmentation in such applications as structure elucidation (25,28-31) and mixture analysis (23,24). It is also possible to emulate the MIKES technique with a normal geometry double focusing mass spectrometer (electric sector preceding the magnet) and a linked scan of both the electric sector field strength and either the magnetic field or accelerating voltage (43).

True tandem mass spectrometers have been constructed to apply selected ion fragmentation techniques to the study of interactions between ions and molecules (10). Two quadrupoles in tandem have been employed to study ion-molecule reactions (11), and triple quadrupole systems have been applied to study the photodissociation of ions (12,13). However, it is the CID process in the center quad that makes the triple quadrupole spectrometer described here particularly well suited for analytical applications.

Description of Instrument

A scale drawing of the triple quadrupole spectrometer appears in Figure 5-3. The path length from source to detector is approximately 67 cm. The individual components of the system, including the source, quadrupoles, detector, vacuum system, and control electronics, are described below.

Samples may be introduced through a heated glass inlet system or a heated direct-insertion probe. The ion source is a Finnigan CI/EI model which operates with 2-200 eV electron energy (70 eV typical) and 0.01-3.0 mA emission current (1.0 mA typical). The reasonably tight source has a measured conductance of approximately 0.5 l/s.

The first quadrupole mass filter is a standard Extra-nuclear Labs ELFS model with 0.95 cm diameter x 20 cm long rods and a mass range of 1-1000 amu. The center quadru-pole is a homemade model with 0.954 cm diameter x 21.6 cm long stainless steel rods mounted with Delrin collars in a stainless steel cylinder. Conductance is approxi-mately 4 l/s. Peak RF voltage of 0-150 V (35 V pRF typi-cally) can be applied to the quadrupole from a solid state power supply constructed from the plans of the Denver Research Institute (44). Flat plate lenses on each end of the center quadrupole aid in focusing the ion beam between quadrupoles. Another Extranuclear mass filter serves as the third quadrupole. It is identical to the

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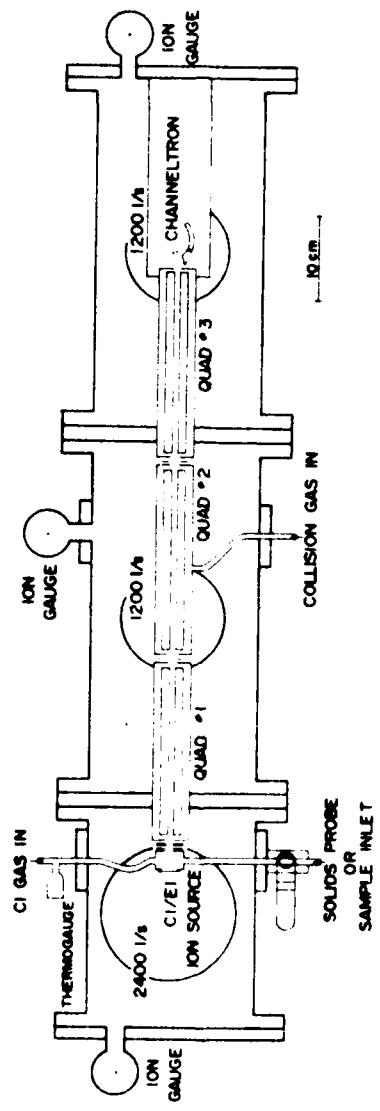
Figure 5-3. Scale drawing (top view) of triple quadrupole
mass spectrometer.

first except that the small (0.2 cm diameter) entrance aperture has been removed. The axial ion energy in the three quadrupoles may be varied independently over the range -100 to +100 V, with -10 V being typical for positive ions.

The positive ions are detected with a Galileo 4770 high-current Channeltron with a measured gain of 3×10^6 at -3 kV. The multiplier is mounted off axis to eliminate noise from stray neutrals and photons, with a deflection electrode at -65 V which helps to focus the ions into the Channeltron. The multiplier is interchangeable with a 4870 Channeltron which has a gain that is sufficient (3×10^8) to allow ion counting for positive and negative ions. The current from the multiplier is detected with a Keithley 18000-20 picoammeter with programmable ranges of 10 V/10^{-10} A to 10 V/10^{-3} A.

The components of the mass spectrometer are enclosed in three differentially pumped stainless steel chambers, each pumped by an oil diffusion pump with water-cooled baffle (see Figure 5-3). Normal operating pressures in the three chambers, as indicated by ion gauges, are source chamber: EI 2×10^{-7} torr, CI 6×10^{-4} torr; center chamber: 2×10^{-6} torr (no collision gas); detector chamber: 2×10^{-6} torr. Source pressures up to 10 torr are possible but 1 torr is typical in CI mode. Source pressure is measured by a Granville-Phillips Thermogauge on the CI gas line. Collision

gas pressures from 2×10^{-6} torr to 1×10^{-2} torr are possible. The ion gauge on the center chamber is calibrated against a thermogauge mounted on the center quadrupole in order to provide routine measurement of the collision gas pressure.

The entire vacuum system is interlocked to provide fail-safe operation and permit computerized cycling of the vacuum system. Foreline pressures, coolant water flow, electric current through the pumps, pneumatic pressure, and valve position are all monitored and used to control the proper sequencing of all pumps, electropneumatic valves, and electronics.

Data acquisition from the system is currently either manual (strip chart recorder or oscilloscope), or automated with an Intel SDK-85 microprocessor, CRT terminal, and floppy disc. A multiple microprocessor system employing the Intel 8085 is currently under development for data acquisition and intelligent control of the instrument. The entire system has been designed for computer control, including the mass selection in both mass filters, the selection of mass filter or total-ion mode, the RF voltage on all three quadrupoles, the control of collision and CI gases, and the vacuum interlock. The capabilities of the triple quadrupole system for selected ion fragmentation will be significantly enhanced under complete computer control.

Performance of Instrument

The use of quadrupoles as mass filters and as the CID
chamber has provided the anticipated excellent selectivity
and sensitivity. Selectivity is achieved by tandem mass
separation up to mass 1000 with resolution as high as one
part in 1500. The high sensitivity (detection limit of
10^{-15} mole) results from the very efficient low-energy CID
process and the high transmission of each component along
the ion path.

Resolution

The two mass filters have been operating with a mass
range of 1-500 amu (2.8 MHz RF), but the maximum mass is
being increased to 1000 amu (1.9 MHz RF). The ultimate
resolution of the quadrupoles is approximately 1 part in
1500, as determined by measuring peak width at half height.
As an example of the resolving power, the N^+/CH_2^+ doublet
at 14 amu can be resolved (50% valley), which requires a
resolution of 1 part in 1100. The mass filters can be
operated in two modes: constant resolution and resolu-
tion proportional to mass. At constant resolution (e.g.,
1 part in 1000 over entire mass range) the relative abun-
dance of the ions in a mass spectrum closely resembles
that observed with double-focusing mass spectrometers.
With resolution proportional to mass (e.g., 1 part in 100

at mass 50, 1 part in 1000 at mass 500), the intensity of
the low mass peaks is enhanced. The quadrupoles are
typically operated with unit mass resolution (1% valley)
over the entire mass range. The peak broadening due to
kinetic energy loss on fragmentation that is observed with
MIKES instruments does not occur with the quadrupole mass
filter.

CID Efficiency

The high sensitivity of the triple quadrupole system
is a result of the high efficiency of each component.
The ion source and lenses produce approximately 1 ion for
every 2×10^5 molecules, as determined by measuring the ion
current entering the first quadrupole at a known sample flux.
The mass filters have a transmission efficiency of approxi-
mately 60% in RF-only mode, and 10% in mass filter mode
with resolution of 1 part in 200. The center quadrupole
has virtually 100% transmission. Even more important is
the efficiency of the CID process which occurs in the
center quadrupole. In an earlier demonstration of the high
efficiency of the low-energy CID process in a triple quad-
rupole system (2), three expressions were developed to
describe the efficiency. The collection efficiency is
the ratio of ions exiting the quadrupole to those entering.
With no collision gas present, there is 100% collection.
At 2×10^{-4} torr collision gas pressure, the collection

efficiency ranges from 50% for light ions like $CH_4^+\cdot$ up to 75% for heavier ions which are less prone to scatter. The strong focusing of the quadrupole field minimizes scattering losses. The fragmentation efficiency is the fraction of the ions exiting the center quad that are fragment ions. At 2×10^{-4} torr, fragmentation efficiencies range from 15% to 65% for various compounds (2). As the collision gas pressure is increased, the fragmentation efficiency for all compounds approaches 100% due to multiple collisions, but the collection efficiency decreases due to scattering. The overall CID efficiency, which is the product of the collection and fragmentation efficiencies, exhibits a maximum at some intermediate pressure. The collection efficiency as a function of collision gas pressure for the dissociation of $CH_4^+\cdot$ from methane is shown in Figure 5-4. The fragmentation efficiencies for the production of the CH_3^+ and $CH_2^+\cdot$ ions are also shown.

Several other factors besides collision gas pressure can affect the efficiency of the CID process (2). The larger the molecular diameter of the collision gas, the more efficient the CID. Ion axial energy and ion internal energy also affect the CID process. A more detailed study of these effects is in progress.
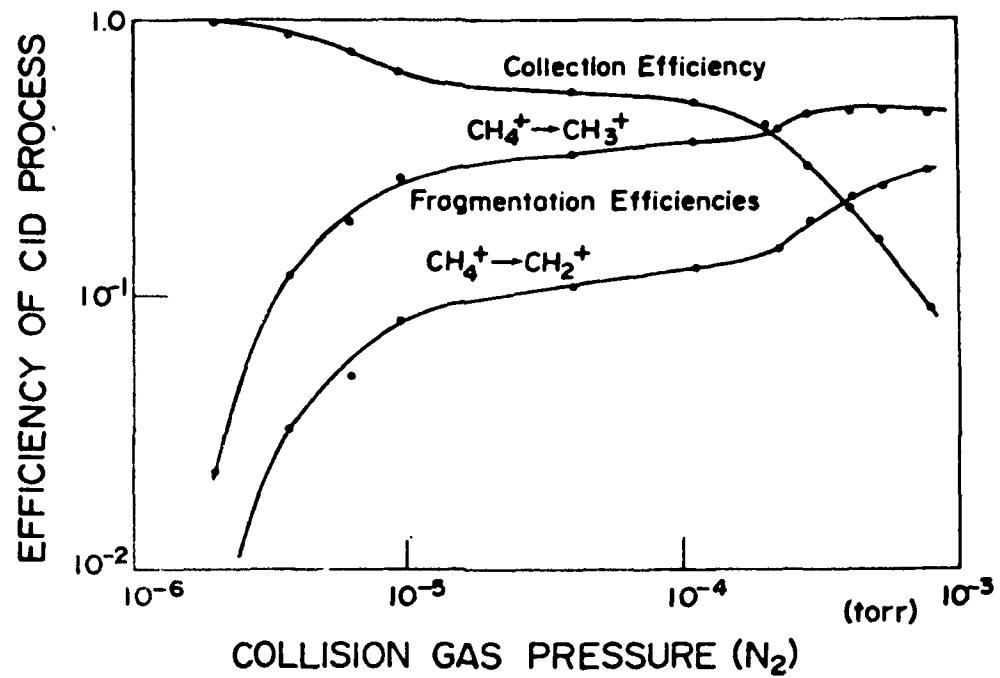
Figure 5-4. Effect of collision gas (N_2) pressure on CID efficiency for methane CH_4^+ at ion axial energy of 10 eV.

Sensitivity

The overall sensitivity of the instrument can be estimated from the product of the efficiencies of the individual processes. The source efficiency and the transmission through the three quads (without collision) are 2×10^{-5} and 10^{-2}, respectively. The fragmentation efficiency is a function of the ion and fragment selected, but for $CH_4 \cdot \rightarrow CH_3^+$ from Figure 5-4 it is seen to be about 0.1. The overall efficiency is 2×10^{-8}, _i.e._, two CH_3^+ ions reach the detector per 10^8 CH_4 molecules passing through the source. The detection system can measure the current due to one ion per second which is an average current of 5×10^{-13} A. For methane, then, a current of 4×10^{-10} A will be produced from a sample flux of 1 pg per second.

The ultimate detection limit depends on the system sensitivity, the chemical and electrical noise levels, and the lowest measurable signal level. The electrical noise in the system is typically 3×10^{-13} A. The two stages of mass separation often make it possible to reduce chemical noise (ions detected from other than the desired reaction) to well below the 10^{-13} A level. In such a case, at the extreme sensitivity limit, the peak height is quantized depending upon the integer number of ions reaching the detector during the scanning time of the peak. The detection of 4 ions would give an S/N of 2 and, for methane, would require, 6 fg of sample. The detection

limit for methane has been determined experimentally to be 16 femtograms by measuring a sample of 10 ppm CH_4 in N_2 at a sample flux of 20 femtograms per sec of CH_4. The large excess of N_2 is required to increase the ion source pressure so that it can be accurately measured and the sample flux calculated. The selectivity of monitoring the $CH_4^+ \rightarrow CH_3^+$ reaction has effected a two order of magnitude improvement in detection limit compared to that obtained by simply monitoring the CH_4^+, CH_3^+, or CH_2^+ ions from electron impact. This improvement is due to the elimination of the chemical noise introduced by background $^{14}N^+$, $^{15}N^+$ and $^{16}O^+$ peaks.

The selected ion fragmentation capability of the instrument produces only a small loss in transmission and sensitivity, and produces a significant gain in selectivity. Indeed, in the normal case where the system is limited by chemical rather than electrical noise (23), a substantial improvement in detection limit can be achieved as was observed for methane. The detection limit of approximately 10^{-15} mole is made possible by the high efficiency of every component of the system.

The detection limit for a higher mass organic compound, nitrobenzene, has also been determined experimentally. The transition $NO_2C_6H_5^+ \rightarrow C_6H_5^+$ was monitored at unit mass resolution in both mass filters, with the parent ion produced by electron impact on a sample of 10 ppm nitrobenzene in N_2. A detection limit of 120 femtograms (S/N=2)

was obtained with a sample flux of 200 femtograms/second.
In contrast, for the MIKES technique, Cooks has estimated
a detection limit of 10 pg for the $140^+ \rightarrow 123^+$ transition
of protonated nitrophenol ions produced by CI (45). Al-
though consumption of only femtograms is required for re-
cording the single reaction, actual sample size is signifi-
cantly larger than this and is dependent on the sample
inlet used. Total consumption of a sample introduced by
direct probe should make it possible to detect quantities
of individual components at close to these detection limits.

Structure Elucidation

As an example of a structure elucidation application,
consider unknown 5.13 in McLafferty's classic text (46)
on mass spectral interpretation. The EI spectrum shows
molecular weight 120 with major peaks at 105 and 77. Con-
sidering the 77 peak (phenyl moiety) and 105 (loss of
methyl), there are two possible compounds, $C_6H_5COCH_3$
and $C_6H_5CH(CH_3)_2$. Relying on the 121/120 ratio and the
unusually small hydrogen-loss ions from 120 and 105, Mc-
Lafferty concludes that the unknown is acetophenone,
$C_6H_5COCH_3$. The structure of this unknown can be obtained
in a direct manner using selected ion fragmentation on the
triple quadrupole mass spectrometer. The large 43^+ peak
in the EI spectrum corresponds to the remainder of the
molecule $[CH_3CO^+$ or $(CH_3)_2CH^+]$ after loss of 77 (C_6H_5).

The CID spectrum of 43^+ is shown in Figure 5-5. Interpretation of the data indicates the fragmentations shown for CH_3CO^+. Comparison with reference CID spectra of known ions, as shown in Figure 5-5, shows a nearly perfect match with the CID spectrum of CH_3CO^+ from acetone. Thus, McLafferty's conclusion is confirmed. The process of structure elucidation of this unknown has been made simpler and more reliable by the added information available by selected ion fragmentation.

Conclusions

The CID process performed in the strong focusing field of an RF-only quadrupole is efficient and effective in producing characteristic spectra of selected ions. The independence of the mass filtering operation on kinetic energy is ideal for collision product analysis. Independent control of the two mass filters provides easy implementation of the various analytical modes.

The system can be used to detect species present in a mixture including isomers without prior separation at the 10^{-15} mole level. The capability to select a desired initial mass and specific collision product mass reduces chemical noise dramatically. For structure elucidation applications, the spectra of selected functional moieties in the molecule may be obtained. A number of other
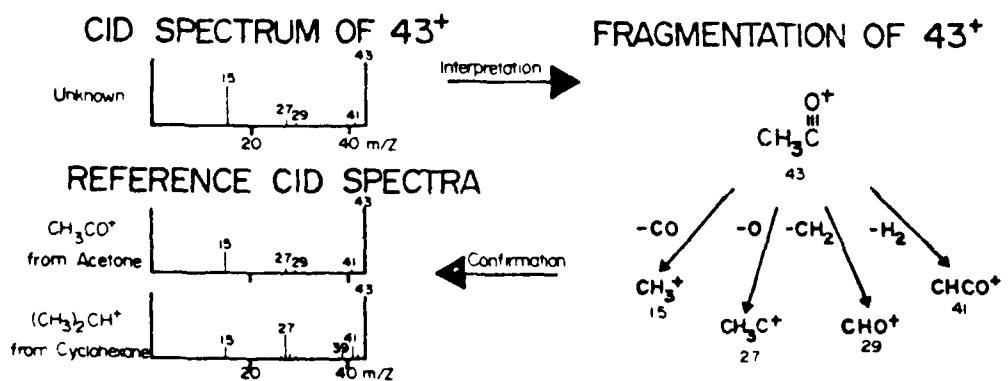
Figure 5-5. Structure elucidation of 43[+] functional moiety by interpretation of CID spectrum and comparison with reference CID spectra.

applications of the selected ion fragmentation technique
are promising, including the analysis of isotopically
labelled samples, in which the first mass filter can
eliminate interferences from molecules that are not com-
pletely labelled.

CHAPTER 6

FUTURE WORK

The triple quadrupole mass spectrometer has been
demonstrated to be a simple and efficient instrument for
mixture analysis and structure elucidation. A number of
projects remain to be undertaken in the further refinement
of the instrument and the technique, the extension of
chemical applications, and the quest to better understand
the low-energy CID process.

A number of instrumental improvements and additions
are advisable. The mass range of the quadrupoles needs
to be extended to 1000 amu. The addition of ion counting
should increase the precision and convenience of measuring
low-level ion signals. The addition of negative ion detec-
tion will open up important new areas of study. Improve-
ment in the efficiency of the ion source is an important
step in improving the instrumental sensitivity. The direct
insertion probe for the introduction of solid samples should
be completed and tested. The development of the multiple
microprocessor system and the interfacing of the triple
quadrupole instrument to it is undoubtedly the most im-
portant project yet to be accomplished. The analytical
capabilities of the system will be fully realized only

under complete computer control.

The low-energy CID process needs to be further characterized in order to better understand and apply it to analytical applications. In particular, the collision gas pressure in the center quadrupole must be more accurately measured. Studies of reactions of known cross section and simulation studies of the ion collision process should help in this characterization process.

Finally, the applications of the triple quadrupole system should be extended into new areas. More complex mixtures and real-life samples must be analyzed. Computerized mass spectral interpretation and pattern recognition need to be implemented for real-time structure elucidation of unknowns. The selected ion fragmentation technique must also be applied to new types of chemical problems such as the identification of isotope substitution.

The research described in this thesis has demonstrated dramatically the potential of the triple quadrupole mass spectrometer for chemical analysis. The future research proposed here should help realize this potential and further expand the horizons of triple quadrupole mass spectrometry.

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## Selected Ion Fragmentation with a Tandem Quadrupole Mass Spectrometer

Sir:

An added dimension of mass spectral information is provided by a tandem mass spectrometer when it is used to create ion species from a sample, select one individual ion species, fragment it, and obtain the mass spectrum of the fragments. Metastable ion peaks and collision-induced dissociation (CID) have been used to relate daughter ions and their precursors.[1] Specialized "MIKES"[2] instruments have been developed to allow systematic acquisition of data on metastable and CID fragmentation spectra. The potential of such instruments for mixture analysis and structure elucidation is currently being explored. These processes are illustrated in Chart I. The second

Chart I

Sample	Ionization	Mass Sep'n	CID Fragment'n	Mass Sep'n	Detection
M	M^+, D^+, R^+	M⁺ D⁺ R⁺	A⁺, a⁺, c⁺	A⁺ B⁺ C⁺	STRUCTURE DATA
K,M,N	K^+, M^+, N^+	M⁺ N⁺	M⁺, Q⁺, R⁺	M⁺ Q⁺ R⁺	MIXTURE DATA
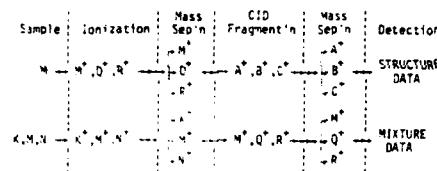
mass separation in MIKES instruments is actually an ion kinetic energy separation interpreted to provide the fragmentation mass spectrum. Impressive sensitivity has been achieved with a MIKES instrument[3] despite the substantial ion losses and the ion energy spread produced by the CID process.[4-6]

Data presented here demonstrate that a selected ion fragmentation mass spectrometer based on tandem quadrupole mass filters is completely practical and that the CID process in the quadrupole instrument is effective and extremely efficient. The system consists of, in series, an electron impact (EI) ionization source, a quadrupole mass filter, an "RF-only" quadrupole CID region, a second quadrupole mass filter, and an electron multiplier. The use of quadrupoles for mass separation provides higher transmission efficiency than magnetic sectors operated at the same resolution and mass range,[7] and unit mass resolution in the CID spectra is easily obtained.

Tandem quadrupole mass spectrometers have been developed for the study of ion-molecule reactions.[8-10] A center RF-only quadrupole has been added for photodissociation studies[11,12] and the investigation of long-lived metastable ions.[13] Prior to this study, however, all of the reported selected ion fragmentation work has been performed on reversed-sector MIKES instruments.[1,3-6,14]

Experiments demonstrating the practicability of selected ion fragmentation in a quadrupole system have been performed on a tandem quadrupole mass spectrometer[12] in the laboratory of J. D. Morrison at LaTrobe University, Bundoora, Victoria, Australia. The central quadrupole of three was used as the CID chamber by the admission of the collision gas and operation in the RF-only mode. The EI source sensitivity was 3×10^{-5} A/Torr of cyclohexane (1 ion/10^5 molecules). Transmission through the ion optics into the first quadrupole was 30%. In RF-only mode, quadrupole transmission was 30%. In mass filter mode, transmission dropped to 2.5%. Neglecting CID, this gives an overall sensitivity of 1.5×10^{-9} A/Torr of cyclohexane (5 ions detected/10^{10} sample molecules). The selected ions emerged from the first quadrupole and entered the CID quadrupole with a translational energy of 10 V. The RF oscillations of the ions in the CID quadrupole increase the ion energy by a few volts. However, the kinetic energy of ions in these experiments is very small compared with that of MIKES
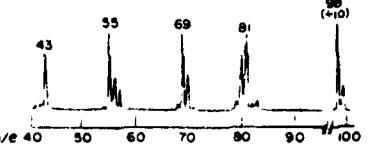

Figure 1. CID spectrum of the parent ion (m/e 98) of cyclohexanone present as 5% of a mixture.

instruments where ions enter the CID chamber with an energy of 3–10 kV. The CID spectra obtained in the quadrupole instrument resemble the 14–16-eV EI spectra of the pure compounds. Clearly the low translational energy combined with the relatively long ($\sim 5 \times 10^{-5}$ s) residence times of the ions in the CID region is sufficient to provide a characteristic and relatively rich fragmentation spectrum.

The efficiency of the CID process is determined by two factors, the fragmentation efficiency and the collection efficiency. We can let P_0 and P symbolize the selected ion beam current at the entrance and exit of the CID region, respectively, and ΣF_i the total current of all fragment ions at the exit of the region. The fragmentation efficiency is $E_F = \Sigma F_i/(P + \Sigma F_i)$, the collection efficiency is $E_C = (P + \Sigma F_i)/P_0$, and the overall CID efficiency is $E_{CID} = \Sigma F_i/P_0 = E_F E_C$. The overall CID efficiency of the quadrupole system ranges from 15% for benzene to 65% for *n*-hexane. The CID efficiency of a MIKES instrument has recently been reported as <10%.[1] The collection efficiency in the tandem quadrupole system is nearly 100%; there is virtually no scattering loss in the CID process, even at the 2×10^{-4} Torr CID pressure used in these studies. (Larger pressures could not be obtained with this instrument.) In this system, CID occurs in a strong-focusing quadrupole field: the field-free drift region used for CID in MIKES instruments produces scattering losses of 90% (collection efficiency of 10%) at similar CID pressures.[14]

The scattering losses in the MIKES CID chamber increase as the mass of the collision gas increases. This has led to a preference for hydrogen or helium as the collision gas.[6,14] Because the collection efficiency is nearly 100% in the quadrupole CID region, heavier collision gases can be used to increase the fragmentation efficiency. Argon shows CID efficiencies three to four times higher than hydrogen in this system.

To demonstrate the mixture analysis capabilities of the quadrupole system, a mixture of cyclohexane and three minor components (benzene, *n*-hexane, and cyclohexanone, each present as 5% of the mixture), was analyzed. The mixture components were selected to minimize interference between fragment ions and molecular ions in the EI spectrum of the mixture. This, of course, would not be necessary if a low energy ion source such as chemical ionization (CI) were used. The CID spectrum of the parent ion of each of the four components was obtained; that for cyclohexanone is shown in Figure 1. The CID spectra of all of the mixture components are reproducible and show good agreement with the CID spectra of the pure compounds. On the basis of these results, the probability of being able to achieve a highly effective, yet fundamentally simple, quadrupole-based selected ion fragmentation mass spectrometer seems virtually certain.

A tandem quadrupole system for selected ion fragmentation is currently under construction in this laboratory. It will have a dual CI/EI source and more efficient quadrupoles with a larger mass range and be able to tolerate higher CID pressure than the instrument on which these experiments were performed. The ability to vary the translational energy of ions entering the CID region will also be incorporated. This instrument will be used to further characterize the low-energy

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CID process and to explore selected ion fragmentation applications in mixture analysis and structural elucidation.

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(2) MIKES (mass-analyzed ion kinetic energy spectrometry), DADI (direct analysis of daughter ions), and CAMS (collisional activation mass spectrometry) all refer to the technique in which kinetic energy analysis in the second (electric) sector of a reversed-sector double-focusing mass spectrometer is used to provide mass data on metastable or CID ions.
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APPENDIX B

HIGH EFFICIENCY COLLISION-INDUCED DISSOCIATION IN AN RF-ONLY QUADRUPOLE

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ABSTRACT

Collision-induced dissociation (CID), when performed in an RF-only quadrupole is a highly efficient method of fragmenting ions. The low-energy (5—10 eV) CID process may involve direct vibrational excitation by momentum transfer but, in any case, is a very different process from the high-energy (3—10 keV) electronic excitation CID process observed in MIKES and CAMS. Experimental results are presented which demonstrate the efficiency of CID fragmentation (up to 65%), the elimination of scattering losses, and the effects of varying such experimental parameters as choice and pressure of collision gas, ion velocity in the quadrupole, and quadrupole RF voltage and frequency. The appearance of the CID fragmentation spectra is roughly similar to 14-eV EI spectra. The results of digital simulation of ion trajectories in an RF-only quadrupole are presented. The correspondence between simulated and experimental results aids in the understanding of the quadrupole CID process. The high efficiency of the CID process in an RF-only quadrupole is significant in the development of a tandem quadrupole mass spectrometer for selected ion fragmentation studies.

INTRODUCTION

One of the most exciting areas in mass spectrometry is selected ion fragmentation, in which an ion is mass-selected, fragmented, and the resulting fragment ions are mass-analyzed. Collision-induced dissociation (CID) has received considerable interest recently as a fragmentation technique for selected ion fragmentation. These studies have been performed on reversed-geometry double-focussing mass spectrometers at ion kinetic energies of 3—10 keV by several groups, see for example Kondrat and Cooks [1] and Mc-

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Lafferty and Bockhoff [2], under labels such as MIKES, CAMS, and DADI *. We have investigated the selected ion fragmentation technique using a very different implementation, i.e. a triple tandem quadrupole system [3]. In this system, CID occurs in the center quadrupole operated in an RF-only (total ion) mode, and at ion kinetic energies of 5—20 eV. At these low energies, the CID process may involve vibrational excitation by momentum transfer, but in any case is quite different from the high-energy CID process observed in MIKES, which involves electronic excitation [4].

Experiments show that the low-energy quadrupole CID process is characterized by very efficient fragmentation (conversion of up to 65% of the ions into fragments) and the virtual elimination of ion losses even at collision gas pressures of 2×10^{-4} torr. The CID spectra obtained show some similarity to the low-energy (12—20 eV) electron impact (EI) spectra of the corresponding molecules. The efficiency of the induced fragmentation and the degree of fragmentation (relative abundance of fragments which have higher appearance potentials) in the CID spectra are affected similarly by changes in the experimental parameters. Increasing the collision gas pressure or molecular weight increases the induced fragmentation. With the instrument used in these studies, the CID efficiency exhibits a minimum at an ion axial energy of 10 eV. Neither the RF voltage nor frequency on the CID quadrupole has any significant effect on the CID process. These effects can be explained by theoretical and simulation studies of the low-energy CID process in a quadrupole.

EXPERIMENTAL

These experiments were performed on a triple quadrupole system originally designed for studies of laser-induced photodissociation which has been described [5]. A diagram of the system appears in Fig. 1. For these experiments, a collision gas (hydrogen or argon) was introduced into the center quadrupole (1.9 cm diameter rods, 15 cm long). The quadrupole was operated at 2.8 MHz over a range 0—1 kV peak RF. Collision gas pressures up to 2×10^{-4} torr were used; this limit is imposed by the lack of differential pumping between the CID region and the electron multiplier. Collision gas pressures were measured with an ionization gauge and corrected for the specific CID gas. The first and third quadrupoles (0.79 cm diameter rods, 20 cm long) were tuned to provide unit mass resolution over the entire mass range 0—100 u. Samples were introduced through an unheated batch inlet system and ionized typically in an electron impact source with 70-eV electrons.

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* MIKES — Mass-analyzed Ion Kinetic Energy Spectrometer. CAMS — Collisional Activation Mass Spectrometer. DADI — Direct Analysis of Daughter Ions.
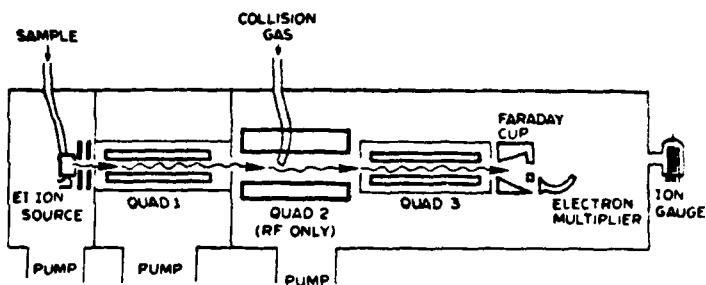
Fig. 1. Diagram of the tandem quadrupole mass spectrometer system showing the center RF-only quadrupole CID region.

SIMULATIONS

The quadrupole CID process was studied using digital simulation of ion trajectories in an RF-only quadrupole. The simulation programs already described [6] operate on a PDP 11/40 minicomputer with 28K words memory, cartridge disk, Tektronix 4010 graphics terminal, and an RT-11 operating system. The simulations assume round rods and a point-by-point description of the field within the quadrupole. Fringing fields are ignored. An ion may be "injected" into the field and its motion traced. The trajectories are observed to resemble ellipses, centered around the quadrupole axis. An example appears in Fig. 2. Ion trajectories for the parameters used in these experiments exhibit much smaller orbits.

Approximate empirical expressions which describe the ion motion have been obtained by observing the effects of each of the variables on the characteristics of the trajectory. Simulations covered the range 100 kHz to 20 MHz, 10–1000 V peak RF, 1–2 cm diameter rods, and ions of mass 5–600. The expressions thus obtained for the period and path length of the generally elliptical orbits (and hence average velocity), as well as the upper and lower mass limits, appear in Table 1. Note especially that the ion's average transverse velocity (and hence the path length through the quadrupole and transverse kinetic energy) is independent of the RF voltage and frequency. Neither RF parameter should then affect the CID process, as is experimentally observed.

Other experiments have been performed to test the validity of the simulation results in Table 1. Measuring the transmission of ions with m/z 15, 28, and 41 from cyclohexane as a function of peak RF voltage gives a value of 0.4 for the constant in the expression for M_{min}, the lower mass limit. In comparison, the stability diagram for the mass filter [7] predicts $M_{min} = (0.3\ V)/(f^2\ d^2)$. The upper mass limit is experimentally too indistinct to compare with the simulated expression. The period of the ion orbit may be

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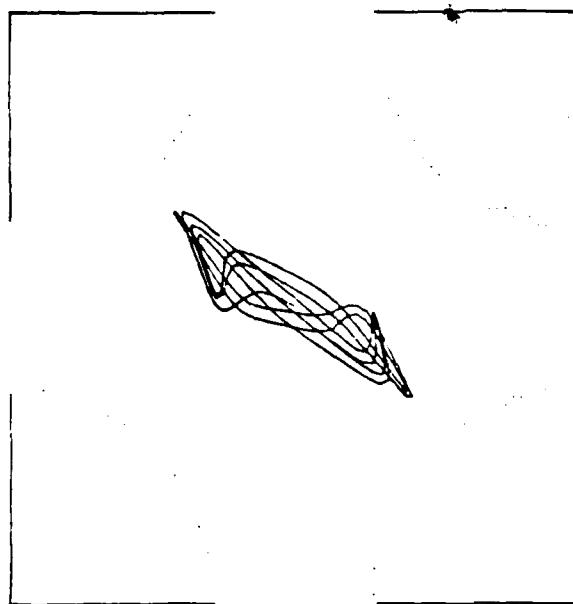
Fig. 2. Simulated ion trajectory. Ion m/z = 36. Peak RF voltage = 25 V. RF frequency = 0.35 MHz. Diameter of rods = 1.9 cm. Off-axis energy = 1 eV. Time = 40 μs.

experimentally determined. Under certain operating conditions, the maximum excursion of the ions from the axis of the quadrupole is large compared to the exit aperture. In this case the signal exhibits a maximum whenever the ions have executed an integral number of half-orbits (that is, they

TABLE 1

Expressions describing simulated ion trajectories in RF-only quadrupoles [*]

Orbit period	$\tau = \dfrac{6 \times 10^{-6}\ m f d^2}{V}$	(s)
Orbit length	$l = \dfrac{5 \times 10^{-2}\sqrt{mE}\ f d^2}{V}$	(m)
Average velocity	$\bar{v} = \dfrac{l}{\tau} = 9 \times 10^3 \sqrt{E/m}$	(m s^{-1})
Lower mass limit	$M_{min} = \dfrac{0.5\ V}{f^2 d^2}$	(u)
Upper mass limit	$M_{max} = \dfrac{2 \times 10^{-2}\ V^{5/2}}{f^2 d^2 E}$	(u)

[*] V = Peak RF voltage (V); f = RF frequency (MHz); E = off-axis energy (eV); m = ion mass (u); d = pole diameter (cm).

are near the axis of the quadrupole) as they reach the end of the quadrupole. By changing the RF voltage, frequency, or ion mass and observing the resultant beat patterns in the ion signal, the dependence of the orbit period on these experimental parameters can be determined. Experimentally, the orbit period appears to obey the relationship $\tau = (7 \times 10^{-6}\ mfd^2)/V$, a result which is quite close to the expression for the simulated behavior. The period of the fundamental ion motion can be calculated from the theory [7], and can be approximated for an RF-only quadrupole by $\tau = (7.5 \times 10^{-6}\ mfd^2)/V$. The validity of the trajectory simulations is demonstrated by the agreement between the simulated results and both the experimental and theoretical values. The usefulness of the simulations is proven by the assistance they provide in understanding the quadrupole CID process.

CID EFFICIENCY

The efficiency of the CID process is determined by the efficiency of fragmentation and the efficiency of collection of the ions. We can let P_0 and P represent the parent ion beam current at the entrance and exit of the CID region, respectively, and ΣF_i the total current of all fragment ions at the exit of the region. The fragmentation efficiency is $E_F = \Sigma F_i/(P + \Sigma F_i)$, the collection efficiency is $E_C = (P + \Sigma F_i)/P_0$, and the overall CID efficiency is the product $E_{CID} = E_F \cdot E_C = \Sigma F_i/P_0$.

The collection efficiency in the quadrupole CID region is virtually 100%. There is no detectable loss of ions owing to scattering, neutralization, or similar mechanisms at pressures up to 2×10^{-4} torr. The strong focussing nature of the RF-only quadrupole stabilizes the ion after collision and fragmentation. Preliminary simulation studies show that the ion trajectories after collision and fragmentation may contract, but do not get larger. Similar results have been seen for simulated collisions in a three-dimensional quadrupole [8].

Fragmentation efficiency in the quadrupole CID system for the compounds studied ranges from 15% for benzene to 65% for n-hexane. This corresponds to fragmentation cross-sections of 9×10^{-16}–1×10^{-14} cm^2. At pressures of 2×10^{-4} torr, the mean free path (assuming an ion collision diameter of 5 Å) is approximately equal to the length of the CID quadrupole, 15 cm. The actual ion path length through the CID quadrupole is approximately one-and-a-half times the length of the quadrupole owing to the ion's oscillations in the RF field. While transversing 1.5 mean free paths, approximately 87% of the ions experience one or more collision, 47% two or more, and 26% three or more. In the case of the n-hexane, in which 65% of the parent ions are fragmented, 75% of the collisions must lead to fragmentation. This very high efficiency of the low-energy CID process is a very clear indication that the low-energy collisions do not follow the Massey "adiabatic criterion" [9] which gives the limit for the maximum energy transfer in high-energy collisions.

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TABLE 2

Effect of ion axial voltage on fragmentation efficiency *

Ion axial voltage (V)	$\Sigma F_i/(P + \Sigma F_i)$
0	0.22
2.5	0.19
5	0.17
10	0.15
15	0.45

* Cyclohexane 84* parent ion. Argon CID gas at 2×10^{-4} torr. Peak RF voltage = 72 V. Ion axial voltage in first and third quadrupoles = 11 V.

Although the collection efficiency remains nearly 100% under all experimental conditions, the fragmentation efficiency is strongly influenced by changes in experimental variables such as collision gas species and pressure and ion axial energy (see Table 2). Experiments on the triple quadrupole system show that argon produces fragmentation efficiencies three to four times greater than those measured when hydrogen is the collision gas. At the low energies used in the quadrupole system (5—20 eV), CID may occur through vibrational excitation by momentum transfer [4]. Hence the more massive argon atoms would be expected to be more efficient for low-energy CID than hydrogen. At the high energies used in MIKES systems (3—10 keV), CID occurs by vertical electronic excitation followed by relaxation
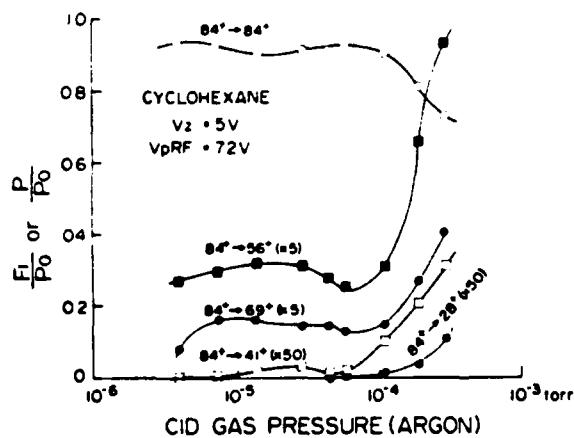

Fig. 3. Relative intensity of the parent ion (P/P_0) and individual fragment ions (F_i/P_0) as a function of CID pressure (argon) for cyclohexane 84*. Ion axial voltage = 5 V. Peak RF voltage = 72 V.

into vibrational excitation [4]. In this light it is not surprising that some workers find hydrogen or helium to be most efficient for CID in MIKES systems [10,11]. The use of a light collision gas undoubtedly reduces scattering in the field-free drift region used for CID in MIKES systems.

Fragmentation efficiency increases as the CID pressure is increased. The effect of the argon collision gas pressure on the intensity of the 84° parent peak and the individual fragment ions of cyclohexane is shown in Fig. 3. The intensity of all the fragment ions increases dramatically above 10^{-4} torr. Future experiments will extend these studies above the 2×10^{-4}-torr limit of the system at La Trobe. For a first-order dependence of the CID process on collision gas, we would expect plots of $\ln(P/P_0)$ vs. pressure or $\Sigma F_i/P$ vs. pressure to be linear. The quantity and precision of the current data are not sufficient to confirm or refute the hypothesis of a first-order fragmentation process.

The axial energy of the ions as they pass through the CID quadrupole has a marked influence on the efficiency of fragmentation. The fragmentation efficiency exhibits a minimum at an ion axial voltage of 10 V. At higher axial voltages, the increased kinetic energy of the ions leads to more energetic collisions and therefore more efficient fragmentation. At ion axial energies below 10 eV, the kinetic energy of the transverse motion of the ions as they oscillate in the RF field (about 5 eV according to the simulations) is the main source of collision energy. Although the collision energy is lower, the lower ion axial velocity increases the number of orbital oscillations the ion undergoes through the quadrupole, and this increased path length results in more collisions. We did not initially expect that the fragmentation efficiency would be nearly independent of the RF voltage and frequency. However, this experimental observation is supported by the simulations, in which the ion's transverse velocity (and hence the total path length and ion kinetic energy) is independent of the RF voltage and frequency.

In summary, the overall CID efficiency may be increased by (1) increasing the mass of the collision gas molecules, (2) increasing the CID pressure, or (3) increasing or decreasing the ion axial voltage from 10 V. The efficiency of the CID process is independent, however, of both the frequency and peak RF voltage on the CID quadrupole.

APPEARANCE OF CID SPECTRA

A very important factor in assessing the usefulness of CID as a technique for selected ion fragmentation is the appearance of the resulting mass spectra. Examples of the CID spectra obtained are presented in Fig. 4. The spectra of n-hexane and benzene demonstrate the characteristic and relatively rich spectra seen.

An estimate of the amount of energy involved in fragmentation may be obtained by comparing the CID spectra with electron impact spectra. High-energy MIKES CID shows similarities between CID spectra and 50-eV EI

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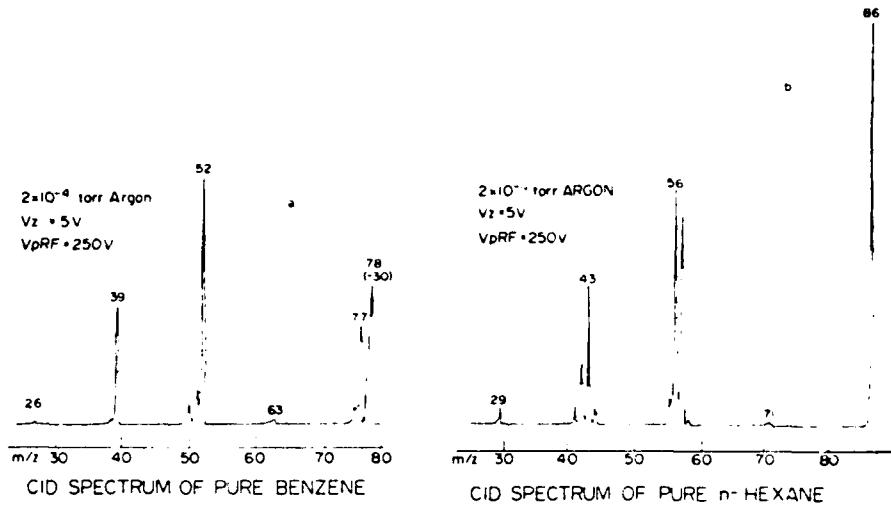
Fig. 4. CID spectra of (a) benzene 78⁺ and (b) n-hexane 86⁺. Argon CID gas at 2 x 10⁻⁴ torr. Ion axial voltage = 5 V. Peak RF voltage = 250 V.

spectra [12]. In the quadrupole system, however, we are observing a very different CID process. The CID spectra obtained resemble 12—20-eV EI spectra, with 14 eV being typical, although differences in the relative abundance of some fragments are apparent.

The abundance of the CID fragment ions can also be compared with the differences between the appearance potentials of the normal ions and the ionization potential of the parent ion. The CID spectra and appearance potential of the corresponding ions for benzene and n-hexane are presented in Table 3. Note that the intensity F_i of the fragment ions generally shows a correlation with the appearance potentials; the greater the appearance potential, the lower the intensity.

The effects of the experimental parameters of the quadrupole CID system on the appearance of the spectra follow closely the effects seen on CID efficiency. Increasing the mass of the collision gas or increasing the ion axial voltage above 10 V increases the intensity of the ions of higher appearance potentials (that is, increases the electron energy in the corresponding EI spectrum). Increasing either of these variables produces more energetic collisions. Increasing the collision gas pressure, or decreasing the ion axial voltage below 10 V also increases the intensity of ions of higher appearance potentials, since either change increases the number of collisions and the probability of multiple collisions. It would not be expected that the change due to more multiple collisions would be the same as that due to more energetic colli-

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TABLE 3

Comparison of CID spectra [a] and ion appearance potentials

m/z	AP−IP (eV) [b]	CID [c]
Benzene		
77	4.6	18
76	5.0	3
52	5.3	45
39	5.5	22
63	6.5	11
50	8.3	4
51	8.4	6
26	9.8	0.3
27	9.9	0.1
n-Hexane		
71	0.9	0.4
70	0.8	0
57	0.8	30
56	0.8	32
42	0.8	8
43	1.1	19

[a] 2×10^{-4} torr argon CID gas. Ion axial voltage 5 V. Peak RF voltage 250 V.
[b] Appearance potential (AP) for normal ion minus ionization potential (IP) for molecular (parent) ion. Benzene data from ref. 13, n-hexane data from ref. 14.
[c] Total fragment ions = 100.

sions, but more complete data will be necessary to make that comparison. Neither RF voltage nor frequency have a noticeable effect on the appearance of the CID spectra.

CONCLUSIONS

It has been demonstrated that the triple quadrupole system using CID at low energies in a center RF-only quadrupole is a simple, efficient system for selected ion fragmentation. Quadrupole CID shows a high fragmentation efficiency (up to 65%) and essentially 100% collection efficiency. The low energy CID process is different in several significant aspects from the high-energy process employed in MIKES.

Digital simulation of ion trajectories in an RF-only quadrupole have been shown to be in good agreement with quadrupole theory and with experimental data. Results of the simulation are a valuable aid in understanding the quadrupole CID process.

A triple quadrupole system for selected ion fragmentation has recently been completed at Michigan State University. It will enable us to extend these studies to higher masses, tolerate higher CID gas pressures, control the ion axial voltage over a wide range, and fragment ions that are generated by

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chemical ionization as well as electron impact. The new system will allow us to more completely characterize the low-energy CID process and investigate its application to mixture analysis and structure elucidation.

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